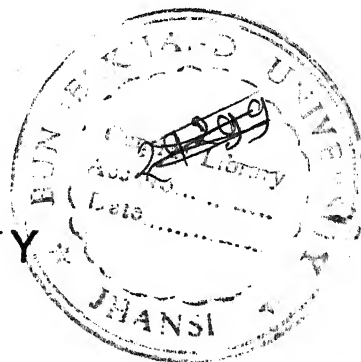


Evaluation of Changes in Lipid Lipoprotein Profile
Induced After Ingestion of Single High-Cholesterol
Test Diet in Subjects of Endocrine and
Metabolic Disease, Chronic Liver Disease,
Chronic Renal Insufficiency and Chronic
Obstructive Pulmonary Disease.

THESIS
FOR
DOCTOR OF MEDICINE
(**MEDICINE**)



BUNDELKHAND UNIVERSITY
JHANSI (U. P.)

C E R T I F I C A T E

This is to certify that the work entitled "EVALUATION OF CHANGES IN LIPID LIPOPROTEIN PROFILE INDUCED AFTER INGESTION OF SINGLE HIGH CHOLESTEROL TEST DIET IN SUBJECTS OF ENDOCRINE & METABOLIC DISEASE, CHRONIC LIVER DISEASE, CHRONIC RENAL INSUFFICIENCY AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE" which is being submitted as a thesis for M.D.(Medicine) Examination, 1993, Bundelkhand University, has been carried out by Dr. Samir Swami, in the department of Medicine, M.L.B. Medical College, Jhansi.

He has put in the necessary stay in the department as per university regulations.

Dated: 28th Sept., 1993.




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Professor and Head,
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C E R T I F I C A T E

This is to certify that the work entitled "EVALUATION OF CHANGES IN LIPID-LIPOPROTEIN PROFILE INDUCED AFTER INGESTION OF SINGLE HIGH CHOLESTEROL TEST DIET IN SUBJECTS OF ENDOCRINE & METABOLIC DISEASE, CHRONIC LIVER DISEASE, CHRONIC RENAL INSUFFICIENCY AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE" which is being submitted as a thesis for M.D.(Medicine) Examination, 1993 of Bundelkhand University, has been carried out by Dr. Samir Swami, under my direct supervision and guidance. The techniques and statistics mentioned in this work were undertaken by the candidate himself and the observations recorded were checked and verified by me from time to time.

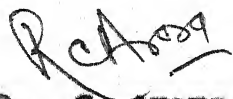
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C E R T I F I C A T E

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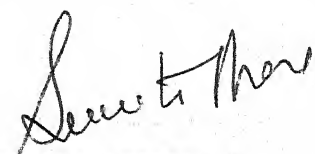

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to lend a helping hand whenever I needed it, despite
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who were the subjects for this study.

Dated: 28th Sept., 1992.


(Samir Swami)

DEDICATED
TO
MY
PARENTS
WITH
ALL LOVE & AFFECTION
FOR
MAKING EVERY THING
POSSIBLE
AND
FOR
MAKING EVERY THING
WORTHWHILE

C O N T E N T S

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I N T R O D U C T I O N

I N T R O D U C T I O N

The clinical importance of plasma lipoprotein level derives from the ability of plasma lipoproteins to cause two life threatening diseases : atherosclerosis and pancreatitis. Among the most important risk factors are hypertension, diabetes, obesity, elevated serum cholesterol, smoking, stress, as well as genetic predisposition. Much is still uncertain about the exact relationship. these risk factors have with each other, and what is their contribution, both singly as well as in combination, to the overall risk. However, an abnormal lipid level is a factor that may be common to several of them. Diet also plays a major role in modifying the effects of the above-mentioned factors, and consequently in determining the lipid profile of both healthy as well as diseased persons. Modification of diet has been shown to result in progression or regression of atherosclerotic lesions in several experimental models (John et al, 1972).

Some hyperlipoproteinemias are the direct result of primary defects in the metabolism of lipoprotein particles. Other hyperlipoproteinaemias are secondary, that is, the elevated plasma lipoprotein level occurs as part of a constellation of abnormalities caused by an underlying disorder in a related metabolic system, such as thyroid hormone deficiency or insulin deficiency. Despite much emphasis being placed on the link between an elevated

fasting lipid lipoprotein level and atherosclerosis, it has also been observed that a large number of normocholesterolaemic subjects are equally affected by the atherosclerotic process. Thus it is evident that fasting lipid levels do not reflect the true risk of an individual.

Indeed, results of recent studies on patients of chronic renal failure (Attmann and Alaupovic, 1990) showed that abnormalities of lipoprotein metabolism leading to dyslipoproteinaemia are present already in the early stages of renal insufficiency, and that these abnormalities are not detected by measurement of plasma lipid. It remains to be established as to what extent these abnormalities of lipoprotein metabolism may contribute to the progression of renal disease and cardiovascular complications. Also, more than forty percent of young patients of documented CAD do not reveal raised fasting cholesterol level (Gregory et al, 1983). Yet they have rampant atherogenous vascular involvement.

Zilversmit (1973) attempted an explanation of this question by postulating that atherogenesis may be a post prandial phenomenon. Transient post prandial rise of beta VLDL, chylomicrons and formation of several species of unusual lipoproteins, may cause repeated cholesterol deposition in cells in arterial walls over the years, while fasting cholesterol values may remain well within normal range over the same duration. Thus it seems logical that post prandial responses of an individual to high cholesterol fat load may

be more closely related to his risk of developing atherosclerosis in future. Moreover, these responses may be dependent upon, or modified by the basal lipid profile of an individual, which, in the case of diseased persons, may be at a considerable variance from normal. As a corollary, it follows that diseased persons may have a vastly increased or decreased risk for developing atherosclerosis as compared to normal persons, depending upon both their basal lipid profile as well as the post prandial changes induced in it following a high cholesterol fat load. Both these parameters can be a unique function of either the individual, or the disease process, or an interplay of both these influences upon the lipid profile. Therefore, it was considered appropriate to concentrate the present study on disease states associated with an abnormal lipid lipoprotein profile.

Proper evaluation and definition of these responses and correct interpretation may perhaps be the first major step towards formulation of a cholesterol tolerance test. Previous efforts in this direction by several other workers (Albrink and Man, 1956; Pomerance, 1954) were inconclusive, primarily because each of them calculated serum total cholesterol and other lipid subfractions 2-6 hours after a test load, presuming that cholesterol is a slowly absorbed substance and therefore, cannot produce alterations of serum cholesterol levels before two hours.

The identification of LDL receptor by Joseph Goldstein and its role in control of serum cholesterol

metabolism, has greatly enhanced our understanding of cholesterol turnover. Cholesterol now no more remains such an inert substance as thought before. In fact, disappearance of intravenous radio-active cholesterol within 20 minutes of injection, from the vascular compartment reflects its high dynamic state with the tissue cholesterol. Perhaps this dynamic equilibrium is achieved by the presence of LDL receptors and as yet undefined hormonal or neurogenic reflexes affecting those receptors.

Previous studies in our department (Arora et al, 1989) have demonstrated that acute changes in serum total cholesterol (STC), low density lipoprotein (LDL) and serum triglycerides (STG) occur after a single high cholesterol test load in both healthy and disease (Arora RC & Sharma S, et al) subjects. Majority of the healthy population showed a fall in serum total cholesterol and LDL level at one hour, while diabetics, first degree relatives of ischaemic heart disease patients, and a minority of healthy population display a rise in serum total cholesterol and LDL levels at one hour. Further studies on hypertensives diabetics and ischaemic heart disease patients (Arora RC, Agarwal, N and Singh DK, 1990) revealed that all three groups showed a higher ratio of STC/HDL (75), particularly ischaemic heart disease patients, in which STC/HDL ratio was more than 7.

Since prolonged feeding is not applicable on a mass scale for screening purposes, so we decided to study

postprandial changes in lipid profile after ingestion
of single high cholesterol test load in diseased persons.

AIMS OF STUDY

1. To analyze the fasting serum lipids/lipoproteins in cases of endocrine and metabolic disease, chronic liver disease, chronic renal insufficiency and chronic obstructive pulmonary disease.
 2. To analyze the changes induced after feeding of single high cholesterol fat diet in patients of above mentioned diseases.
-

REVIEW OF LITERATURE

REVIEW OF LITERATURE

The relation between the levels of dietary and serum cholesterol has attracted the attention of the scientific community since Anichkov's cholesterol feeding experiments in rabbits at the beginning of this century.

Recent research has revealed a rather complex set of events that control plasma lipoprotein level. Specific proteins have been implicated in the regulation of lipoprotein synthesis. Besides this, many more factors like age, sex, smoking, obesity, hypertension, dietary habits and sedentary life style exert their influence on lipoprotein levels and development of atherosclerosis in their own way. Many of the risk factors are reversible but influences of age, sex and genetic factors are irreversible.

A single high cholesterol diet induced change in various subfractions of lipid lipoproteins and its relevance in predicting an individual's risk for future atherosclerosis still remains an unexplored field. The discovery of cell surface receptors for low density lipoprotein (LDL) by Dr. Joseph Goldstein, was fundamental to our understanding of how plasma cholesterol levels are controlled.

CHANGES IN LIPID LIPOPROTEIN LEVELS AFTER HIGH CHOLESTEROL DIET

The effect of feeding cholesterol over a long term or short term period evokes variable responses and is subject to individual variation. Dietary fat and

cholesterol causes changes in specific lipoprotein in a variety of species (Mahley et al, 1978; Arora et al, 1987). Quantitatively, a change in specific lipoprotein may be dramatic in one species while insignificant in another.

CHANGES IN TOTAL SERUM CHOLESTEROL

In 1956 Ancelkeys and Anderson et al concluded that serum cholesterol level is essentially independent of the cholesterol intake over the entire range of natural human diets. But later on it was proved beyond doubt that feeding cholesterol rich diet for 2-8 weeks raises total serum cholesterol in blood (Arora et al, 1987; Mesinger et al.; Conner et al, 1961; Deborah Applebaum et al, 1979).

In a recent study, (Martha and McMurry et al, 1991) a group of thirteen Tarahamara Indians (a Mexican people known to consume a low fat high fibre diet and to have a very low incidence of risk for coronary heart disease) consumed their traditional diet (2700 Kcal per day) for one week, and were then fed a diet typical of affluent societies, which contained excessive calories (4700 K cal per day), total fat, saturated fat, and cholesterol. After 5 weeks of consuming the affluent diet, the subjects' mean (\pm S.E.) plasma cholesterol level increased by 31 percent from 121 ± 5 to 159 ± 6 mg%. The increase in plasma cholesterol level was primarily in the low density lipoprotein fraction, which rose 39 percent from 72 ± 3 to 100 ± 4 mg%. HDL cholesterol, usually low in this population, increased by 31%.

An effect of dietary cholesterol in raising serum cholesterol levels has also been demonstrated in metabolic ward experiments and in some but not all studies of free living subjects. In studies by Connor and Connor (1989) serum cholesterol was increased by a dietary cholesterol intake upto approximately 400 to 500 mg/day; a higher intake had a minor additional effect. These findings imply that the efficiency of cholesterol absorption decreases as the amount of dietary cholesterol increases.

Recently, McNamara reviewed the data from 68 clinical studies published over a span of nearly 30 years. He found fairly consistent results, averaging an increase in serum cholesterol of 2-3 mg/dl (0.06 m mol/l) for each 100 mg increase in dietary cholesterol - quite different from the changes of 9.6 and 6.8 mg/dl (0.25 and 0.18 m mol/l) predicted by the classic Hegsted and Keys formulae, which describe linear and square root relations, respectively, between cholesterol consumption and serum cholesterol levels.

In an earlier report, Bruhn (1940) observed a 20% rise in mean cholesterol level after a fat load. Effect of high cholesterol fat load on post prandial cholesterol levels have also been studied in the past by several workers, but insignificant difference has been found between post prandial and 10 to 14 hours fasting value (Albrink and Man, 1956; Pomeranze et al, 1954, Schilling et al, 1964). All these workers observed plasma cholesterol values upto 24 hours after a test meal. On the other hand Nikkila and

Konttinen (1962) demonstrated a significant decrease in cholesterol level six hours after a fat diet in healthy soldiers.

Hanno Krauss, Pieter Groot (1987) reported insignificant changes in total serum cholesterol after feeding 0.5 gm/M^2 of cholesterol and taking readings at 2 hourly interval for 14 hours.

In adolescents with initial cholesterol levels greater than 200 mg/dl, a 50 percent decrease in cholesterol intake led to an appreciable drop (15.6%) in cholesterol levels, but the effect was much more modest (8.3%) in those with lower initial levels (Gandey et al, 1972).

In another large survey of school children, there was no positive correlation between the low (80-130 mg/dl) the intermediate (157 to 180 mg/dl) and the high (194 to 425 mg/dl) cholesterol levels with the mean daily intake of energy, sugar, fat, saturated fat and cholesterol (Weidman et al, 1978). However, in 7 different studies, summarised recently, significantly weak correlations were noted between serum lipids and dietary P/S ratio (Mellies and Glueck, 1983).

Textured vegetable proteins lowered total serum cholesterol in hypercholesterolemic subjects with no change or slight elevation in HDL cholesterol, no effect or only minor changes have been observed in normolipidaemic subjects (Sirtori et al, 1985).

The replacement of animal protein with vegetable protein in the diet has been suggested to reduce the diet

linked atherogenic risk (Carroll, 1982).

However, Sacks et al (1983) found no appreciable correlation between total intake of protein, when consumed above minimum requirement and serum cholesterol level.

Work in animals showing that sucrose and fructose are atherogenic prompted human studies, which have not shown consistent changes. In one study isocaloric replacement of starch with sucrose in mixed diet did not lead to changes in serum cholesterol (Mann and Truswell, 1972), changes that were documented in another study (Reider et al, 1978).

HIGH DENSITY LIPOPROTEINS (HDL)

High density lipoproteins are lipid lipoprotein complexes defined by flotation in the ultra centrifuge between density 1.063 and 1.21 gm/ml, by the presence of major protein constituents, apolipoprotein A-I and A-II, and by alpha migration on electrophoresis. Three classes of HDL are separated on the basis of flotation rates on ultracentrifugation; HDL₃ have flotation rates between 0-3.5, HDL₂ have rates in excess of 3.5. The third and minor HDL₁ is sometimes found at d \geq 1.063 and overlaps with the low density lipoprotein distribution. Recently Mahley and colleagues have identified a distinct sub type of HDL designated as HDLc or apo E-HDLc. This is found in the plasma of cholesterol fed animals and to a much smaller extent in human fed high cholesterol, high saturated fat diets. HDLc differs from other sub type by presence of

apolipoprotein E. This property confers an affinity for the low density lipoprotein receptor (Mahley and Weisgraber, 1978).

The lipid constituents of HDL exhibit variations. Cholesterol ester content may range from 10-20 percent, triglycerides are normally less than 4 percent. The ratio of cholesterol to triglycerides in HDL may show wide fluctuations with increase being observed after dietary cholesterol supplementation (Mistry et al, 1977) and decrease being found in patients with hypertriglyceridemia (Weisweiler et al, 1977), Uremia (Brunzell et al, 1977) and Ischaemic Heart disease (Carlson et al, 1975).

Conflicting reports have appeared on effect of dietary cholesterol on HDL levels:

Borden et al (1964) reported enhanced levels of HDL-c in rats fed cholesterol while Haft et al (1962) and Kritchevsky (1965) reported no change in HDL levels in cholesterol fed rats. Reiser et al (1966) and Howard et al (1968) reported decreased level of HDL cholesterol in rats fed with high cholesterol diet.

Narayan (1971) demonstrated that HDL₂ decreased drastically - about 50% in rats fed with high cholesterol diet. These results confirmed the earlier observations of Reiser et al (1966) that rat serum HDL level was decreased irrespective of whether a saturated or unsaturated fat was used in the diet supplemented with cholesterol. In short term feeding studies, marked reduction in dietary fat and isocaloric increase in carbohydrate resulted in decrease

in HDL cholesterol in conjugation with elevation of serum triglyceride and VLDL. Studies of HDL composition have shown a decrease in ratio of apolipoprotein A-I to A-II and a decrease in HDL cholesterol to protein ratio (Schonfeld et al, 1976) consistent with a selective decrease in HDL₂ species (Blum et al, 1977).

There is evidence that substitution of large quantities of poly-unsaturated fat for saturated fat in diet can result in lower levels of HDL lipids and proteins (Nichaman et al, 1967). An increase in the P/S fat ratio from 0.25 : 1 to 4 : 1 in food diet fed to four normal subjects for five weeks resulted in reduction of HDL cholesterol and apolipoproteins A-I concentration of 33 and 21 percent respectively, with an associated reduction in HDL₂ : HDL₃ ratio (Shepherd et al, 1978). Other studies have however, reported either no change (Lewis, 1978; Shere et al, 1981) or increase (Jackson and Glueck, 1980) in levels of HDL cholesterol with feeding of diets enriched in poly-unsaturated fats. High dietary intake of cholesterol, in the form of three to six egg yolks per day, has been reported to produce increase in apo-lipoprotein E containing HDL - sub species in human (Mahley et al, 1978). This effect was seen whether or not there was an increase in total plasma cholesterol. Despite the fact that HDL containing apolipoprotein E represented only a minor fraction to the total HDL its presence was shown to account for an increase of 2.6 to 4 times the

binding of HDL to LDL receptors of fibroblasts as compared to pretreatment HDL (Mahley et al, 1981). But this was not observed in another study (Applebaum et al, 1979). Recently it has been reported that level of HDL cholesterol and serum apolipoprotein A-I but not apolipoprotein E increased with the feeding of diets high in both cholesterol and saturated fat (Tan et al, 1974).

A final consideration in evaluating the effects of dietary variables on HDL is that, while levels of HDL cholesterol and plasma apolipoprotein A-I are similar after overnight fast and non fasting states (Henderson et al, 1980), changes in levels and composition of HDL have been shown to occur acutely after meals containing fat. Cholesterol phospholipid and C-apolipoprotein levels in HDL₂ increases and cholesterol in HDL decreases (Havel, 1973; Baggio et al, 1980) in conjunction with transfer of chylomicron lipids to HDL during the course of their catabolism. Recently, it has been shown that HDL apolipoprotein A-I levels increased when fat was consumed in divided doses over a 10 hour period but not when the same amount of fat was ingested as a single load (Kay et al, 1980).

LOW DENSITY LIPOPROTEIN CHOLESTEROL (LDL-c)

More than 75 percent of the total cholesterol present in the plasma is in the form of LDL-c. LDL-c is generated by the degradation and removal of triglyceride from very low density lipoprotein (VLDL) in the plasma.

Their density is in the range of 1.019 to 1.063 and they contain apoprotein B 100.

In 1977, Goldstein hypothesized the concept of LDL receptor. The presence of these receptors have been confirmed by many laboratories. LDL receptors are present on the cell surface of liver, adrenal cortical cell, lymphocytes, muscle cells and renal cells. LDL that binds to this receptor is taken up by the receptor mediated endocytosis and digested by lysosome within the cells. The cholesterol esters of LDL are hydrolyzed by a lysosomal cholesteryl-esterase and the liberated cholesterol is used both for membrane synthesis and as a precursor for steroid hormone synthesis. Liver uses the LDL-c for synthesis of bile acids and for generation of free cholesterol which is secreted into the bile.

Diets high in fat and cholesterol cause an elevation in LDL in most animals (Mahley, 1978). The response in man varies, but in those subjects who have an elevation in plasma cholesterol, there is an elevation in plasma LDL levels. In 1979 Deborah-Applebaum et al demonstrated significant rise of LDL level in human volunteers after feeding 5000 mg of egg yolk cholesterol per day for 30 days.

Age related difference in rise of LDL was demonstrated by Arora and Gupta G (1987). They found that rise of total serum cholesterol after feeding high fat high cholesterol breakfast for one week was much more pronounced in young volunteers with major portion of rise being contri-

buted by increased HDL. In contrast, in the older age groups, the rise of total serum cholesterol was less marked with LDL-c contributing mainly towards the increased levels.

Baudet et al (1981) demonstrated that there was significant fall in level of LDL in five volunteers, three and five hour after taking a butter diet. They attributed this fall to a defect in VLDL hydrolysis by serum lipases and due to metabolic blocking in liver or adipose tissue.

An additional alteration in LDL, induced by feeding high cholesterol diets involves the apoprotein constituents. In normal LDL the B-apoprotein is the major detectable apoprotein moiety. However, in several species, the LDL contains a variable amount of the E apoprotein following cholesterol feeding (Mahley et al, 1977; Rudel et al, 1979).

MECHANISMS FOR CONTROL OF PLASMA CHOLESTEROL LEVELS

Research till date has established a central role for lipoprotein receptors in regulating plasma cholesterol metabolism and transport. The homeostatic and regulatory mechanisms that maintain a relatively constant level of plasma cholesterol despite changes in dietary cholesterol intake include alterations in the efficiency of intestinal absorption and in the rates of cholesterol biosynthesis, LDL receptor activity, secretion of cholesterol into bile and hepatic conversion of cholesterol into bile acids, the chief metabolic product of cholesterol (Mistry and Miller et al, 1981; McNamara et al, 1987).

Cholesterol absorption is a complex process involving a number of steps. Although the rate limiting step is not known with certainty, it is currently believed to be the transport of micellar free cholesterol from the intestinal lumen through the unstirred water layer and, in molecular form across the cell membrane of the enterocyte. This had classically been thought to occur by passive diffusion, but several studies suggest a role for as an yet unidentified brush border protein. Decreased absorption in the presence of increased dietary cholesterol serves as a major control mechanisms in cholesterol hemeostasis, but there is a great individual heterogeneity (Quiñao et al, 1971). Miettinen and Kesäniemi et al (1988) cite the increased absorption of exogenous cholesterol by persons with apolipoprotein E₄ as contributing to the heterogeneity in response to dietary cholesterol.

Another major adaptive mechanism is the rate of conversion of dietary cholesterol to bile acid and the loss of either cholesterol or bile acid in the stool. In 1972, Lofland et al found that hyporesponsive monkeys had increased biliary excretion of cholesterol. Recently Fred Ker^{III} et al (1991) studying a case of a normocholesterolemic 88-year old man who had been consuming 25 eggs a day for the last 15 years reported that the rate of bile acid synthesis in the patient was greater than in any of the 200 subjects studied by them for the last 13 years.

ROLE OF LDL RECEPTORS

Operationally, the LDL/LDL-receptor system can be considered the primary transport mechanism for endogenous cholesterol. LDL are generated in the plasma by the degradation of intermediate density lipoprotein (IDL). Generated LDL is removed relatively slowly from the plasma by binding to LDL receptors in the liver and extra hepatic tissues (Kita et al, 1982). In rabbits, rats and hamsters, more than half of the total LDL receptors are located in the liver. However, the precise distribution of these receptors in man is unknown.

REGULATION OF HEPATIC LDL RECEPTOR

Hepatic LDL receptors are suppressed whenever the liver's content of cholesterol increases or its demand for cholesterol is reduced. Thus receptor suppression occurs when a high cholesterol diet is consumed (Hui et al, 1981), or when bile acids are infused (Angelin et al, 1983). Conversely, LDL receptors increase when hepatic cholesterol synthesis is blocked by the drugs compactin or mevastatin (Goldstein et al, 1982; Belheimer et al, 1983), when bile acid binding resins are given (Shepherd et al, 1980), or when an ileal bypass is created (Spengel et al, 1982). Fasting has also been shown to suppress the LDL receptor in rabbit (Goldstein et al, 1982). LDL receptors can be stimulated by thyroxine (Thompson et al, 1981). Hepatic LDL receptors decline when rabbits are fed a diet composed only

of sucrose and casein (Chao et al, 1982). All these changes in receptor activity alter the rate of uptake of LDL by the liver and cause reciprocal changes in plasma LDL levels. Whenever hepatic LDL receptors are suppressed, the plasma LDL level rises, conversely, whenever, these receptors are induced, the plasma LDL level falls.

TRIGLYCERIDES AND VERY LOW DENSITY LIPOPROTEIN (VLDL)

The level of serum triglyceride (STG) rises considerably after fat ingestion. Rise in the triglyceride level after fat ingestion has been reported after giving different amounts of fat load and measuring the blood level at different intervals thereafter (Nikkila and Kontinen, 1962; Danborough et al, 1963). Angerwall (1963) has reported a significant correlation between fasting, 3/2 hours and 7/2 hours values of serum triglyceride postprandially.

Clefsky et al (1976) noted a biphasic plasma triglyceride curve with an initial peak occurring 1 to 3 hours after feeding and a second peak after 4 to 7 hours. The primary peak was accounted for by increase in chylomicron levels in more than 98% cases, whereas secondary peak represented a rise in VLDL level in 82% of the cases. Previously however, Havel et al (1957) had concluded that increment in the concentration of triglycerides in the serum following ingestion of fat is entirely the result of an increase in their concentration in VLDL.

Excess production of VLDL and triglycerides is more often due to secondary abnormalities than to primary

factors, perhaps the most common cause is high caloric intake associated with obesity, excess alcohol and excess carbohydrate. Increased levels are also found in diabetes mellitus, nephrotic syndrome and hypothyroidism with obesity. Delayed clearance of triglyceride from the serum is noted in cases of ischaemic heart disease after high fat diet (Arora et al, 1987, David et al, 1961).

VLDL REMNANTS

In addition to a report by Mistry et al (1976) that beta VLDL can be induced by cholesterol feeding in man, preliminary studies from the Gladstone Foundation Laboratories for Cardiovascular Disease indicate that certain individuals respond to high fat, high cholesterol diet by producing lipoproteins which are capable of delivering cholesterol to macrophages. The beta VLDL may occur transiently as minor components of the human plasma fractions after diets high in fat and cholesterol are consumed, and may cause repeated cholesterol deposition in cells in the arterial wall over the years. The beta VLDL, either chylomicron remnants or hepatic lipoprotein may represent the atherogenic particle postulated several years ago by Zilver-smit. This alteration in the lipoprotein fraction may represent the most significant diet induced changes in lipoprotein predisposing to accelerated atherosclerosis.

CHYLOMICRONS

Chylomicrons are a means of lipid transport in the

exogenous pathway. They are large lipoprotein particles containing dietary triglyceride and cholesterol. Chylomicrons are rapidly cleared from the plasma and normally are not present after an overnight fast. The detection of these particles in fasting plasma samples, therefore, is always abnormal and may indicate presence of other hyperlipidaemias. Increased levels of chylomicrons in the plasma may be found in cases of genetic defects involving the enzyme lipoprotein lipase and in the familial form of hypertriglyceridemia.

ENDOCRINE & METABOLIC DISORDER AND LIPOPROTEINS

Changes in plasma lipoprotein levels in diabetes remain one of the most important risk factors in terms of accelerated atherosclerosis (Santen et al, 1972). In addition, diabetics may have altered lipoprotein structure and metabolism independent of increase in plasma lipid levels (Eckel et al, 1981; Howard et al, 1978 & Schonfeld et al, 1974), and these altered lipoprotein may be associated with accelerated atherosclerosis. It is generally appreciated that anatomic evidence of accelerated atherosclerosis frequently develops in insulin dependent diabetic patients, ten to fifteen years after onset of diabetes.

Hypertriglyceridemia is the most common lipid abnormality observed in diabetic patients. The main component of hypertriglyceridemia is VLDL and rarely chylomicrons (Nikkila et al, 1973 and 1974). VLDL can cause secondary hypercholesterolaemia. The hypercholesterolemia in diabetes

can occur because :

- a. Increased plasma VLDL level causes a secondary increase in plasma cholesterol levels, since 20% of total lipid content of VLDL is cholesterol.
- b. Diabetes affects the plasma LDL metabolism - the exact mechanism is not clear, but it has been proposed that :
 - (1) the increased synthesis of VLDL in diabetes causes increased LDL formation, since VLDL is a precursor for LDL
 - (2) Decreased catabolism of LDL in poorly controlled diabetes due to glycosylation of plasma LDL (Klitzman, 1982), which alters the configuration of LDL, so that less interaction occurs with specific receptors responsible for the majority of LDL catabolism in normal persons (Brown et al, 1981).

Decreased conversion of VLDL to LDL and impaired LDL clearance are two opposing phenomenon which may influence the LDL concentration of diabetics in either direction. Thus, despite minimal changes in LDL concentration, there are multiple defects in metabolism of LDL in non-insulin dependent diabetes, which may contribute to increased atherogenesis in this disorder (Howard and William et al, 1987).

In the Rockefeller monograph (Allen, 1919), "Lipemia is largely associated with fat intake and other diabetic symptoms", according to Ervin (1919), the lipemia in diabetics will disappear with the elimination of fat from diet. Joslin (1921) suggested a relation between high protein fat diet and a high degree of lipemia, he stated

that with restricted diet, particularly of fat, the blood fat rapidly falls. Bloor (1921) stated that there was a deficiency of pancreatic hormone which is essential for the proper removal of fat from the blood.

Low fat and high carbohydrate in diet : The avoidance of low fat and high carbohydrate in diets of diabetic patients during treatment have been shown to result in lower serum cholesterol, lower insulin requirements, improved glucose tolerance and reduced severity of vascular complications (Ellis et al, 1934; Rabinowitch et al, 1935; Singh et al, 1955; Kampher et al, 1958; and Van Eck et al, 1959). On the other hand, hyperlipidemia has been noted in non diabetics during administration of low fat, high carbohydrate diets. The lipaemic effect of such a diet may be a temporary one. In a study, the reduction of dietary fat over a long period showed that serum triglyceride returned to normal after several months (Autonis et al, 1961).

Recent studies in our department (Arora, Agarwal and Singh et al, 1989) on diabetic subjects given a high cholesterol test diet followed by evaluation of postprandial changes in lipid profile, revealed that one hour after such a meal serum triglyceride levels showed a fall in 40% cases, a rise in 50% cases, whereas remaining 10% cases showed no change. However, these levels were elevated in all cases 3 hours after the test meal. Changes in LDL levels exhibited a similar pattern, while HDL levels did not show any significant alteration, even though the basal HDL levels were higher.

CHRONIC LIVER DISEASE AND LIPOPROTEINS

Hypercholesterolemia and lipoprotein abnormalities have been reported in patients of primary biliary cirrhosis. There is an increased amount of unesterified cholesterol, along with increased levels of chylomicrons, and VLDL. These abnormalities are probably due to hepatic lipase inhibition as well as altered cholesterol esterification in patients of this disease (Jahn and Schaefer et al, 1985).

Manocha et al (1989) analysed fasting plasma samples from 29 patients of cirrhosis, for cholesterol, triglycerides and their lipoprotein fractions. The patients included 11 alcoholic cirrhotics consuming over 130 gm/day of absolute ethanol and 18 non-alcoholic cirrhotics. The difference in lipid values between the two patient groups was not significant except that VLDL cholesterol was raised in alcoholic cirrhotics. However, in comparison to normal healthy controls, the values were significantly altered. The dietary intake in the two groups showed no difference, except that the non alcoholic cirrhotics consumed more animal proteins. Low intake of exogenous fat and reduced synthesis of endogenous cholesterol in cirrhotic patients seemed to influence the total lipid values (Stigendahl and Olsson et al, 1984).

Alcohol ingestion per se has been reported to raise levels of HDL (Johansson et al, 1974; Belfrage et al, 1977). But the results of Glueck et al (1980) were contradictory to the above statement.

In a large epidemiological study, levels of HDL cholesterol and amount of habitual alcohol intake in

moderate range have been independently correlated (Castelli et al, 1977). A recent longitudinal study (Hargreaves et al, 1991) entailing follow up in 1988-89 of men investigated during a study in 1976 revealed that even though alcohol consumption decreased over the 12 years, there was no significant relation between the fall in HDL cholesterol concentration and fall in alcohol consumption.

CHRONIC RENAL INSUFFICIENCY AND LIPOPROTEINS

Abnormalities of lipoprotein metabolism leading to dyslipoproteinaemia are present already in the early stages of renal insufficiency, even though at this early stage, these abnormalities are not detected by measurements of plasma lipids (Attman and Alaupovic, 1990).

Cholesterol ester is the preferred form for cholesterol storage in the liver, since an increase in total hepatic cholesterol is reflected more as esterified than free cholesterol. A possible relationship between cholesterol ester turnover and lipoprotein transport has emerged from the study of Nestel and Associates (1968; 1970). Cholesterol ester turnover has been found to be raised together with triglyceride turnover in subjects with the nephrotic syndrome (McKenzie and Nestel, 1968).

Low plasma HDL cholesterol concentrations in patients with CRF are related to decreases in the synthetic rate of apo A.I/HDL (Martin and Lee et al, 1990). Whereas overproduction of lipoproteins containing apoprotein B is the principal cause of hyperlipidaemia in patients with

the nephrotic syndrome (Joven and Villabona et al, 1990).

Karadi and Romics et al (1989) found that serum lipoprotein (a) levels may be increased in patients of nephrotic syndrome, particularly those with membranous or membranoproliferative glomerulonephritis or primary amyloidosis. But measurements of HDL in patients with the nephrotic syndrome have yielded contradictory results, because lipoprotein (a) floats in the same density range as HDL₂, hence serum HDL concentrations determined solely by ultracentrifugation may be falsely elevated by contamination with substantial amounts of lipoprotein-(a) (Kostner et al, 1983). However, the composition of plasma cholesterol esters is only minimally affected, by a single meal of a specific fat (Kayden et al, 1963), but is readily influenced thereafter.

Patients with chronic renal failure (CRF) tend to have lower than normal plasma HDL cholesterol concentrations (Lewis et al, 1966; Rapoport and Aviram et al, 1978; Goldberg and Harter et al, 1983), although the mechanism responsible for this defect has not been defined. Decreases in HDL cholesterol are often associated with increases in plasma VLDL-TG concentration (Schaefer et al, 1978; Fuller and Pinney et al, 1978) and in two of these instances - endogenous hypertriglyceridemia and NIDDM - it has been shown that the HDL catabolic rate is faster than normal (Saku et al, 1985; Golay and Zech et al, 1987). Hypertriglyceridemia also occurs in patients with CRF, but whereas

patients with endogenous hypertriglyceridemia and NIDDM have an increase in VLDL-TG synthetic rate, a decrease in VLDL-TG synthetic rate is seen in patients with chronic renal failure (Reaven & Swenson et al, 1980). Thus it seems possible that the abnormality in HDL kinetics might also be different in patients with chronic renal failure. Recent studies (Martin and Lee et al, 1990) provided support for the view that low plasma HDL cholesterol concentrations in patients with CRF are related to decreases in synthetic rate of apo A-I/HDL.

There is also evidence that patients with CRF have a factor in their plasma which inhibits lipoprotein lipase (LPL) activity (Murase et al, 1975) and it has also been shown that the lower the LPL activity, the lower the plasma HDL cholesterol concentration (Nikkila and Taskinen et al, 1978).

Patients with CRF are at an increased risk for coronary artery disease (Lindner and Charra et al, 1974) as are patients with NIDDM and endogenous hypertriglyceridemia. None of these clinical syndromes are characterized by an increase in plasma LDL cholesterol concentrations, suggesting that some other mechanism must account for the increased prevalence of coronary artery disease. An obvious contender for this role is the decrease in plasma HDL cholesterol concentration seen in patients with CRF, NIDDM or endogenous hypertriglyceridemia. In this context, it seems worth emphasizing that patients with CRF have a low plasma

HDL cholesterol concentration and a slower than normal fractional catabolic rate (FCR) of apo A-I/HDL. This combination of defects is in marked contrast to the situation in patients with NIDDM and endogenous hypertriglyceridemia, in whom a faster than normal FCR of apo A-I/HDL is associated with a low plasma HDL cholesterol concentration (Fidge and Nestel et al, 1980; Saku and Gartside et al, 1985). Thus, it is not possible to predict the change in HDL kinetics that will be present in patients with a low plasma HDL cholesterol concentration. These observations focus attention on the relationship between the FCR of apo A-I/HDL, plasma HDL cholesterol concentration, and coronary artery disease. It is generally assumed that it is a defect in reverse cholesterol transport that explains ^{why patients} /with a low plasma HDL cholesterol are at increased risk for coronary artery disease (Miller and Miller, 1975).

CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND LIPOPROTEINS

Specific non-cancer respiratory causes of mortality have been infrequently studied in relation to cholesterol concentration. One of the few ongoing long-term cohort studies, that has been the source of most such data, is the Whitehall study, in which 18,403 men aged 40 to 64 years were examined between 1967 and 1969. Plasma cholesterol concentrations were available in 17,718 of these men.

Subjects with respiratory symptoms had lower cholesterol levels than those without respiratory symptoms, and this was reflected in the relationship between cholesterol concentration and quartile of FEV_1 : respiratory symptoms and low FEV_1 are associated with increased overall mortality as well as mortality from respiratory conditions (Ebi-Kryston, 1988). Subjects who reported that they had experienced unexplained weight loss over the year preceding examination had a mean plasma cholesterol concentration of 0.31 mmol/l lower than those who had not experienced weight loss, and their relative rate of mortality was 1.64. Mortality rates were similarly elevated for lung cancer (1.75) and non cancer respiratory disease (2.6).

These findings are in agreement with those from similar other studies (Kozarevic and McGee et al, 1981; Kagan and McGee et al, 1981; Neaton and Blackburn et al, In press), viz. that respiratory disease mortality has shown inverse associations with cholesterol levels. In the present study also (Smith and Shipley et al, 1992), mortality rates from all respiratory disease, plus the subcategories of bronchitis, pneumonia and other respiratory disease displayed consistent inverse associations with cholesterol level - a trend which remained unaltered even after 15 years of follow up. On the other hand, cholesterol concentration showed a continuous positive relationship with coronary heart disease, which is in agreement with results

from other large cohorts (Tornberg and Holm et al, 1989; Neaton and Kuller et al, 1984). Cancer mortality showed no trend with plasma cholesterol concentration.

However, of the individual cancer sites, only lung cancer demonstrated a consistent inverse trend with cholesterol concentration, but pancreas and liver cancer rates were highest in the lowest cholesterol group. Smoking would be the obvious confounder in the relationship between cholesterol level and lung cancer and respiratory disease mortality. There was however, no suggestion of any association between smoking and cholesterol concentration in this cohort. When cancers were divided into those that have consistently been related to smoking (Doll and Peto et al, 1976; Hammond et al, 1966), and those that have not, the negative relationship with cholesterol was seen only for the former. For the smoking related cancers, the mortality rate was highest in the lowest cholesterol group than in the rest of the population.

It could be argued that if low cholesterol levels predispose persons to respiratory mortality, low cholesterol levels will also predispose persons to respiratory disease before death occurs. If this were the case, then adjusting for the presence of respiratory symptoms would be inappropriate. The present study does not allow examination of the temporal relationship between the development of respiratory morbidity and plasma cholesterol levels. Studies in

humans and other primates have, however, demonstrated that respiratory infections lead to lowered plasma cholesterol levels (Kerttula and Weber et al, 1988; Fiser and Denniston et al, 1972). There are two implications of this. First, repeated respiratory infections are a feature of some forms of chronic respiratory morbidity, which could be responsible for the lower plasma cholesterol levels in patients with chronic obstructive pulmonary disease. Second, patients suffering from respiratory infections at the time of examination would have lowered cholesterol levels and also would be at higher risk for further respiratory infections and death attributed to respiratory disease. This could produce the inverse association between plasma cholesterol level at examination and future respiratory disease mortality. Respiratory disease does, therefore, appear to lead to lowered cholesterol levels, whereas there is no substantive evidence to suggest that the converse occurs.

In the Framingham study, subjects whose serum cholesterol concentrations fell between examinations had elevated mortality rates (Anderson and Castelli et al, 1987), which could have been due to illness causing cholesterol levels to decrease. Falling cholesterol levels, however, could have different biological effects than consistently low levels, and the means of lowering cholesterol levels used in the intervention studies could, by themselves, lead to increased mortality (Davey Smith & Pekkanen et al, in Press).

M A T E R I A L A N D M E T H O D S

M A T E R I A L A N D M E T H O D S

The case material for the present study consisted of male and female patients suffering from (a) Endocrine and/or metabolic disease, (b) chronic liver disease, (c) Chronic renal insufficiency and (d) Chronic obstructive pulmonary disease, attending the OPDs or admitted in the wards of M.L.B. Medical College, Hospital, Jhansi.

An informed consent was taken from all the subjects who were to be included in the study. In each case a detailed history was elicited and a meticulous clinical examination and investigations were carried out, and all basic clinical and biochemical parameters recorded. The subjects were then grouped into the following categories :

GROUP A

Group A consisted of male and female patients of diabetes mellitus, ranging in age from 18 to 67 years. The number of patients included in this group was 13; seven cases were of juvenile onset diabetes and six were of maturity onset diabetes.

GROUP B

The second group consisted of 8 male and female patients of hepatic cirrhosis, ranging in age from 11 to 67 years.

GROUP C

The third group consisted of 9 patients of both sexes suffering from chronic renal insufficiency (nephrotic syndrome, Chronic renal failure etc.). The age range of this group was 16 to 56 years.

GROUP D

This group consisted of ten patients of chronic obstructive pulmonary disease, ranging in age from 53 to 80 years. Incidentally, all patients included in this group happened to be males.

A detailed dietary history was elicited to assess the amount of fat consumed daily and weekly by these subjects in their usual routine diet. Specific consideration was given to record the weekly amount of ghee and its type (saturated/unsaturated), oil and its type, milk and milk products, eggs, and food additives. Any recent change in diet, oral or parenteral medication before and during the study were noted. Hospitalized patients were given the diet from the hospital for one week prior to the test.

Fifty one patients had entered the study, out of which eight could not complete the test because of vomiting of the test diet, and in three cases, because of insufficient quantity or haemolysis of one or more of the blood samples, the complete battery of tests could not be carried out. Therefore, complete data from the remaining

40 subjects were included in the final analysis.

DESIGN OF TEST

All subjects were asked to have their dinner at 6.00 PM on the previous night and not to take anything except water till the next morning. Fasting blood samples were taken at 8.00 AM the following morning in the recumbent posture without producing venuous stasis. After this, they were given a test meal consisting of 2 boiled eggs and 250 ml of sweetened whole fat buffalo milk. This supplied 500-550 mg of egg yolk cholesterol.

Postprandial blood samples were taken 1, 2 and 3 hours after the meal. During the test, the subjects were not allowed to take anything except water. Smoking was prohibited during the test period. Serum was separated within four hours by centrifugation and the following tests were performed.

I. SERUM TOTAL CHOLESTEROL (STC)

STC estimation was done by commercial kits supplied by Ortho Diagnostics.

II. SERUM TRIGLYCERIDES (STG)

Estimation of serum triglycerides was done by commercial kits supplied by Ortho Diagnostics.

III. SERUM HIGH DENSITY LIPOPROTEINS (HDL)

This test was done by using commercial kits supplied by Ortho Diagnostics.

IV. VLDL CHOLESTEROL

VLDL cholesterol was calculated by using the formula derived by Friedwald et. al (1972) :

$$\text{VLDL (mg/dl)} = \text{STG}/5$$

V. LDL CHOLESTEROL

LDL cholesterol was estimated by using the following formula given by Fredrickson DS (1972) :

$$\text{LDL (mg/dl)} = \text{STC} - (\text{STG}/5 + \text{HDL})$$

Statistical analysis of the data was done by using paired 't' test and student 't' test.

O B S E R V A T I O N S

O B S E R V A T I O N S

The present study was carried out on 13 male and female patients of diabetes mellitus (Group A), 8 male and female patients of chronic liver disease (Group B), 9 male and female patients of chronic renal insufficiency (Group C) and ten male patients of chronic obstructive pulmonary disease (Group D).

GROUP A

It comprised of 13 male and female patients of diabetes mellitus in the age range of 18 to 67 years, with a mean age of 38.46 ± 13.28 years, mean weight of 52.11 ± 8.08 kg and mean height of 153.42 ± 8.89 cms. Of these 7 were patients of insulin dependent diabetes mellitus (IDDM) and remaining 6 were of non insulin dependent diabetes mellitus (NIDDM). Their other general characteristics are depicted in Appendix- I.

GROUP B

It comprised of eight male and female patients of chronic liver disease, viz. hepatic cirrhosis, ranging in age from 11 to 67 years, with a mean age of 48.87 ± 18.29 years, mean weight of 49.12 ± 11.82 kgs and a mean height of 150.25 ± 18.37 cms. Their other general characteristics are given in Appendix - II.

GROUP C

It comprised of nine male and female patients of chronic renal insufficiency, ranging in age from 16 to 56 years with a mean age of 35.55 ± 14.2 years, mean weight of 50.35 ± 7.5 kg and a mean height of 153.9 ± 6.27 cms. Their other general characteristics are given in Appendix-III.

GROUP D

It comprised of ten male patients of chronic obstructive pulmonary disease, ranging in age from 53 to 80 years with a mean age of 59.2 ± 10.47 years, mean weight of 53.4 ± 3.43 kgs and a mean height of 159.5 ± 8.64 cms. Their other general characteristics are given in Appendix - IV.

TABLE 1 : Effect of single high cholesterol test diet on mean STC levels in subjects of group A, B, C and D (mg/dl).

Groups (n)	Fasting	After 1 hour	After 2 hours	After 3 hours
A (13)	194.51 ± 53.07	189.01 ± 37.37	192.66 ± 39.90	196.74 ± 32.90
B (8)	159.32 ± 48.34	180.92 ± 65.37	178.42 ± 61.06	179.82 ± 62.04
C (9)	295.02 ± 76.88	305.03 ± 80.93	309.00 ± 82.80	321.63 ± 80.12
D (10)	185.99 ± 50.20	203.26 ± 52.18	193.28 ± 51.65	195.28 ± 46.05

TABLE 2 : Effect of single high cholesterol test diet on mean HDL cholesterol levels in subjects of groups A, B, C and D (mg/dl).

Groups (n)	Fasting	After 1 hour	After 2 hours	After 3 hours
A (13)	40.43 ± 8.80	39.87 ± 8.80	39.83 ± 9.17	39.66 ±10.50
B (8)	27.73 ±12.08	33.54 ±16.67	31.83 ±16.19	31.88 ±16.26
C (9)	53.44 ±19.90	63.44 ±28.95	68.82 ±36.59	74.42 ±38.75
D (10)	38.33 ±11.09	38.31 ± 8.06	35.70 ± 9.06	35.97 ± 8.44

TABLE 3 : Effect of single high cholesterol test diet on mean LDL cholesterol levels in subjects of groups A, B, C and D (mg/dl).

Groups (n)	Fasting	After 1 hour	After 2 hours	After 3 hours
A (13)	119.90 ±42.71	110.83 ±24.73	113.21 ±28.55	112.00 ±24.68
B (8)	102.36 ±32.77	113.80 ±46.34	111.38 ±45.27	110.32 ±42.44
C (9)	144.95 ±36.81	131.56 ±30.18	119.62 ±35.64	118.68 ±32.67
D (10)	129.59 ±37.61	141.61 ±40.22	131.83 ±42.25	131.23 ±38.42

TABLE 4 : Effect of single high cholesterol test diet on mean STG levels in subjects of groups A, B, C and D (mg/dl).

Groups (n)	Fasting	After 1 hour	After 2 hours	After 3 hours
A (13)	170.96 ±67.34	191.54 ±91.37	198.15 ±60.99	225.30 ±59.10
B (8)	146.11 ±71.03	165.74 ±95.74	176.02 ±95.74	188.78 ±102.65
C (9)	482.97 ±173.36	550.40 ±222.69	605.92 ±252.89	642.80 ±250.75
D (10)	90.39 ±24.74	116.64 ±38.09	128.77 ±42.07	140.42 ±42.32

TABLE 5 : Effect of single high cholesterol test diet on mean LDL/HDL ratio in subjects of groups A, B, C and D (Mean±S.D.).

Groups (n)	Fasting	After 1 hour	After 2 hours	After 3 hours
A (13)	3.12 ±1.27	2.96 ±1.28	2.98 ±1.08	3.01 ±1.14
B (8)	4.18 ±1.79	3.99 ±2.13	4.34 ±2.68	4.14 ±2.35
C (9)	3.22 ±1.90	2.66 ±1.80	2.39 ±1.74	2.31 ±1.93
D (10)	3.45 ±0.80	3.74 ±0.93	3.89 ±1.41	3.84 ±1.44

CHANGES IN GROUP AChanges in Serum Total Cholesterol(STC)

The overall mean fasting STC of group A was 194.51 ± 53.07 mg/dl (Table 1). In the first hour after administration of single high cholesterol test diet, it showed a decline (-2.80%), but it started rising again two hours after the meal, and this rising trend was maintained at the end of three hours, with the mean three hour level being slightly higher (+1.14%) than the basal level (Table 12). On statistical analysis, none of the changes were statistically significant ($p > 0.05$) when student 't' test was applied.

Three different types of responses were categorised in STC level changes. In some subjects, there was an increase in STC level in the first hour after taking the test meal. If this increase was more than 5% over the fasting value, this type of response was termed AI. In some subjects, there was a sharp fall in STC level after 1 hour. If this fall exceeded 5 percent of the fasting value, it was termed as A-III. In the remainder of the cases, in whom the variation from fasting levels was less than 5 percent it was termed as A-II response (Table 6).

TABLE 6 : Showing the three different types of responses in 1 hour STC in group A after administration of single high cholesterol test diet and their statistical significance on application of paired 't' test (Mean \pm S.D., mg/dl).

Category (n)	Fasting	After 1 hour	p value
A-I (5)	145.80 \pm 14.84	159.10 \pm 20.22	70.1
A-II (4)	199.37 \pm 20.03	201.55 \pm 24.95	70.5
A-III(4)	250.95 \pm 47.80	213.87 \pm 43.53	70.1

On the basis of the above categorization, there were five cases of type A-I response, whose fasting mean STC was 145.8 \pm 14.84 mg/dl, and their mean 1 hour value of STC rose to 159.10 \pm 20.22 mg/dl. Difference in fasting and 1 hour value was not significant. In the A-II group there were four subjects, in whom the variation was slight and therefore statistically insignificant. In the A-III category there were four subjects, whose fasting and 1 hour postprandial mean STC levels were 250.95 \pm 47.80 and 213.87 \pm 43.50 mg/dl respectively. The difference was statistically not significant.

EFFECT OF TYPE OF DIABETES

Considerable differences were observed in both fasting and postprandial STC levels in subjects of IDDM and NIDDM, as depicted in table 7. There were seven insulin dependent diabetics and six non insulin dependent diabetics in our study. The fasting and all the postprandial mean STC levels were higher in subjects of NIDDM.

The fasting cholesterol level was 236.66 ± 45.10 in the NIDDM subgroup, whereas it was 158.38 ± 25.22 in the IDDM subgroup. This difference was statistically significant ($p < 0.05$) when student 't' test was applied.

There was a striking difference in the trend, as well as the mean STC levels in the postprandial phase between the two subgroups. Patients of IDDM displayed a rise in their 1 hour STC level (162.74 ± 18.45 mg/dl) as compared to their basal level (158.38 ± 25.22 mg/dl). This increasing trend was maintained in the 2 hour mean STC level (164.94 ± 14.98 mg/dl) and was maximal 3 hours after ingestion of the high cholesterol test diet (175.95 ± 14.69 mg/dl) - the 3 hour value representing a rise of 11.09% over the basal value. This difference was however, statistically not significant ($p > 0.05$) when student 't' test was applied.

TABLE 7 : Effect of single high cholesterol test diet on mean STC concentration in two subgroups (IDDM & NIDDM) of group A (mg/dl).

Type of Diabetes (n)	Fasting*	After** 1 hour	After* 2 hour	After * 3 hours
IDDM (7)	158.38 ± 25.22	162.74 ± 18.45	164.94 ± 14.98	175.95 ± 14.69
NIDDM(6)	236.66 ± 45.10	219.66 ± 29.16	255.00 ± 29.10	221.00 ± 32.07

* Denotes difference between the two subgroups is statistically significant ($p < 0.05$) on application of student 't' test.

** Denotes difference between the two subgroups is statistically highly significant ($p < 0.02$) application of student 't' test.

In patients of NIDDM, on the other hand, the mean 1 hour STC level (219.66 ± 29.16 mg/dl) exhibited a decline of 7.18% against the mean basal value of 236.66 ± 45.10 mg/dl for this group. There was a slight rise in the mean 2 hour value, again followed by a slight fall in the mean 3 hour value (221.00 ± 32.07 mg/dl), a decline of 6.62 percent over the basal value. Thus all the three postprandial values were below the fasting value in NIDDM patients, with the decline being maximal at the 1 hour interval. The differences were statistically not found to be significant when the student 't' test was applied.

What is noteworthy is that the fasting and postprandial differences in respective values between IDDM and NIDDM patients were all found to be statistically significant ($p < 0.05$), particularly in the case of 1 hour values, the significance was greater ($p < 0.02$), when student 't' test was applied.

Changes in HDL Cholesterol

The HDL levels in diabetics (both IDDM & NIDDM) was the least variable of all the lipid parameters amongst all disease groups studied (Table 2) except group C. The mean basal HDL level was 40.43 ± 8.8 mg/dl, which decreased slightly after 1 hour of ingestion of test diet (39.87 ± 8.8 mg/dl), a decline of 1.3 percent. The rest of the postprandial values varied by less than 0.5 percent from the 1 hour value (Table 12).

EFFECT OF TYPE OF DIABETES

The differences in HDL values - both fasting as well as postprandial - between IDDM and NIDDM subgroups as depicted in table 8, were also very slight, and none of the differences was statistically significant ($p > 0.05$) on applying the student 't' test.

TABLE 8 : Effect of single high cholesterol test diet on mean HDL concentration in two subgroups (IDDM and NIDDM) of group A (mg/dl).

Type of diabetes (n)	Fasting	After 1 hour	After 2 hours	After 3 hours
IDDM (7)	39.68 ± 7.90	38.28 ± 4.50	38.97 ± 7.76	38.47 ± 8.04
NIDDM(6)	41.30 ± 10.40	41.70 ± 12.51	40.80 ± 11.20	41.05 ± 13.53

Changes in LDL Cholesterol

The overall mean fasting LDL cholesterol level was 119.90 ± 42.71 mg/dl diabetics. This declined to 110.83 ± 24.73 mg/dl one hour after ingestion of test diet (Table 3), a fall of 7.56% over the basal value (Table 12). There was a slight rise at the 2 hour level, again followed by a slight fall at 3 hours, with the 3 hours value being 112.0 ± 24.68 mg/dl, representing a fall of 6.5 percent over the fasting value. Thus all the three postprandial levels of LDL were below the fasting LDL level, with the decline being maximal at the 1 hour interval. A similar trend was mirrored in the changes seen in STC levels in these patients (Table 1) as well as the NIDDM subgroup (Table 7).

Effect of type of diabetes

The mean fasting LDL level in the IDDM subgroup (91.68 ± 31.13 mg/dl) was lower than the mean for the group as a whole, and considerably lower than the fasting LDL level in NIDDM subgroup (152.81 ± 28.31 mg/dl) (Table 9). This difference was statistically significant ($p < 0.05$). In contrast to the mean for the group as a whole, as well as the NIDDM subgroup, the 1 hour level exhibited a rise in case of the IDDM subgroup (95.42 ± 22.93 mg/dl). This rise however, was not statistically significant as compared to basal value. It was followed by a slight fall at 2 hours, followed again by a rise at 3 hours (99.25 ± 20.80 mg/dl), representing an increase of 8.26 percent over the fasting levels. This increase too was not found to be statistically significant, when compared to the basal value.

TABLE 9 : Effect of single high cholesterol test diet on mean LDL cholesterol concentration in two subgroups (IDDM & NIDDM) of group A (mg/dl).

Type of diabetes (n)	Fasting*	After* 1 hour	After** 2 hours	After 3 hours
IDDM (7)	91.68 ± 31.13	95.42 ± 22.93	92.42 ± 19.02	99.25 ± 20.80
NIDDM (6)	152.81 ± 28.31	128.80 ± 10.82	137.46 ± 14.54	126.88 ± 21.14

* Denotes difference between the two subgroups is statistically significant ($p < 0.05$) on application of student 't' test.

** Denotes difference between the two subgroups is statistically highly significant ($p < 0.02$) on application of student 't' test.

In the NIDDM subgroup, the 1 hour LDL level was 128.8 ± 10.82 mg/dl, exhibiting a fall of 15.7 percent over the basal LDL level for this subgroup (152.81 ± 28.31 mg/dl).

There was a slight rise at 2 hours (137.46 ± 14.54 mg/dl) followed again by a fall at 3 hours (126.88 ± 21.19 mg/dl) - a decline of 16.97 percent over the fasting value (Table 9). Thus, although all the postprandial levels were below the fasting level in the NIDDM subgroup, the trend differed slightly from that seen for the group as a whole, in the magnitude of the fall being greater, and secondly, the maximal decline being seen in the 3 hour value in the NIDDM subgroup (as against the 1 hour level for the group as a whole). This difference was statistically not significant when compared to the basal level. However, the differences between the respective fasting, 1 hour and 2 hours values between the two subgroups was found to be statistically significant ($p < 0.05$), with the difference in the 2 hour value being markedly so ($p < 0.02$). The difference in the 3 hour value was however, not statistically significant.

Changes in Serum Triglycerides (STG)

The mean fasting STG level in group A patients was 170.96 ± 67.34 mg/dl (Table 4). The postprandial levels showed a steady upward trend with the 3 hour level reaching 225.3 ± 59.10 mg/dl, a rise of 31.78 percent over the fasting level (Table 12). This difference was statistically not found to be significant ($p > 0.05$).

Effect of type of Diabetes

Both the basal and postprandial levels were lesser in IDDM patients than in NIDDM patients (Table 10). This difference was statistically significant in the 3 hour values ($p < 0.05$), but not for the other values. In the IDDM subgroup, a steady rise in the post prandial values of STG was exhibited with maximal increase being obtained in the 3 hour levels. However, the percentage rise at 2 and 3 hours was almost twice as great in the IDDM subgroup than in the NIDDM subgroup, with the 3 hour level (191.05 ± 49.25 mg/dl) representing a rise of 41.34 percent over the basal level (135.17 ± 27.42 mg/dl) (as against a 24.69 percent increase over the basal level in NIDDM patients). This difference was statistically not significant ($p > 0.05$). But the percentage rise at 1 hour was twice as great in the NIDDM subgroup (15.47 percent over the basal value, with a level of 245.65 ± 112.78 mg/dl a difference which was statistically not significant) in comparison to the IDDM subgroup, which showed a percentage increase of 7.4 percent (145.17 ± 25.69 mg/dl) over the fasting value.

There was a slight decline in the 2 hour value of STG (233.56 ± 66.35 mg/dl) followed again by a rise in the 3 hours value to 265.26 ± 43.74 mg/dl. Both these changes were statistically not significant.

TABLE 10 : Effect of single high cholesterol test diet on mean serum triglyceride concentration in two subgroups (IDDM & NIDDM) of group A. (mg/dl).

Type of diabetes (n)	Fasting	After 1 hour	After 2 hours	After* 3 hours
IDDM(7)	195.17 ±22.42	145.17 ±25.69	167.80 ±37.99	191.05 ±49.25
NIDDM(6)	212.73 ±78.07	245.65 ±112.78	233.56 ± 66.35	265.26 ±43.74

* Denotes difference between the two subgroups is statistically significant ($p < 0.05$) on application of student 't' test.

Change in LDL/HDL

Group A subjects exhibited a slight decrease in the LDL/HDL ratio as compared to the fasting value, which was 3.12 ± 1.27 . The decrease was evident after 1 hour, when the value was 2.96 ± 1.28 . There was a very slight rise in the 3 hour value to 3.01 ± 1.14 . None of these variations were statistically significant (Table 5). The 3 hours value was lower than the basal value.

Effect of type of Diabetes

No distinct trend was discernible in either subgroup. In IDDM patients, the ratio, showed a slight rise at the 1 hour followed by a slight fall at 2 hour and a rise again at 3 hours, with the 3 hour value being slightly higher than the fasting value (Table 11). None of these changes were statistically significant ($p > 0.05$) when student 't' test was applied.

Overall IDDM subjects had lower fasting and postprandial ratios than patients in the NIDDM subgroup (Table 11), who had a mean fasting ratio of 3.88 ± 1.08 . The postprandial changes in NIDDM subjects exhibited just the opposite trend to that seen in IDDM subjects, with a fall in the first hour ratio (3.45 ± 1.61), followed by a slight rise at 2 hours, and then again a fall at 3 hours to 3.41 ± 1.39 , with the 3 hours value being lower than the basal value. None of these changes proved to be statistically significant when the student 't' test was applied.

TABLE 11 : Effect of single high cholesterol test diet on mean LDL/HDL ratio in two subgroups (IDDM & NIDDM) of group A.

Type of diabetes (n)	Fasting	After 1 hour	After 2 hours	After 3 hours
IDDM(7)	2.47 ± 1.09	2.55 ± 0.83	2.44 ± 0.74	2.67 ± 0.82
NIDDM(6)	3.88 ± 1.08	3.45 ± 1.61	3.61 ± 1.13	3.41 ± 1.39

TABLE 12 : Showing percentage variance (from the fasting level) of the postprandial levels of different lipid lipoprotein fractions in subjects of group A.

Type of lipid	Percentage of change after		
	1 hour	2 hours	3 hours
STC	- 2.80	- 0.90	+ 1.14
HDL	- 1.30	- 1.40	- 1.90
STG	+ 12.03	+ 15.90	+ 31.78
LDL	- 7.56	- 5.57	- 6.50

applying the student 't' test. The difference between the two subgroups was also statistically insignificant.

TABLE 13 : Showing the two different types of responses in 1 hour STC in group B after administration of single high cholesterol test diet and their statistical significance on application of paired 't' test (mg/dl).

Category (n)	Fasting	After 1 hour	p value
B-I (5)	153.42 \pm 43.17	184.22 \pm 73.02	70.1
B-II (3)	169.16 \pm 64.95	175.41 \pm 64.95	70.5

Changes in HDL Cholesterol

The HDL cholesterol level in cirrhotic patients increased after 1 hour of diet intake (Table 2), but thereafter displayed only very marginal changes at 2 and 3 hours after the ingestion of diet : the 1 hour level of HDL represented a rise of 20.9 percent over the basal level (Table 14), while the 2 and 3 hours levels were 14.78 and 14.9 percent higher than basal level respectively. All the above mentioned changes were not found to be statistically significant (p 70.05) on application of student 't' test.

TABLE 14 : Showing percentage variance from the fasting level of the postprandial levels of different lipid lipoprotein fractions in subjects of group B.

Type of lipids(n)	Percentage change after		
	1 hour	2 hours	3 hours
STC	+ 13.55	+ 11.98	+ 12.86
HDL	+ 20.90	+ 14.78	+ 14.90
STG	+ 13.45	+ 20.47	+ 29.20
LDL	+ 11.17	+ 8.81	+ 7.77

Six out of the eight (75%) subjects in the group displayed a rise in the 1 hour level of HDL, while the remaining two did not show any change. However, after two hours, 5 out of 8 subjects (62.5%) displayed a fall in their HDL values as compared to their 1 hour value but in four of these 5 patients, the 3 hour value again demonstrated a rise, while it was unchanged in the 5th patient. Thus the fall in HDL seen at 2 hour appears to be a transient phenomenon in most of these subjects. Interestingly, the three (37.5%) patients who had displayed a rise in their 2 hours level of HDL over the 1 hour level, in all these three, the 3 hour values showed a downward trend, and these three included both the two patients whose 1 hour value of HDL was unchanged from the basal level. However, the above mentioned changes were found to be insignificant statistically.

Changes in LDL Cholesterol

The mean fasting LDL value was 102.36 ± 32.77 mg/dl in group B subjects (Table 3). This rose to 113.8 ± 46.34 mg/dl at 1 hour after ingestion of test diet (a rise of 11.17 percent over the fasting value) but then declined slightly at the 2 and 3 hour intervals. However, all the three postprandial levels were higher than the basal level.

In 5 out of 8 subjects (62.5%), there was a rise in the 1 hour LDL level over the basal level, and

in 4 of these patients (50%), the 3 hour level demonstrated a further rise. Only in one of these five (12.5%) did the 3 hour level drop marginally below the basal level (See Appendix - II).

On the other hand, in the 3 subjects (37.5%) in whom the 1 hour value had declined from the fasting level, in all these three, this downward trend continued at 2nd and 3rd hour and all three had 3 hour levels of LDL below their fasting values. The above mentioned changes were found to be not significant on statistical analysis.

Changes in STG

The mean fasting STG level in group C subjects was 146.11 ± 71.03 mg/dl (Table 4). A sustained rising trend was evident in all the three postprandial levels, with the 3 hour value rising to 188.78 ± 102.65 mg/dl an increase of 29.2 percent over the basal level (Table 14). In 7 of the 8 subjects (87.5%), the triglyceride levels exhibited a gradual and sustained rise from the basal values, with the 3 hour values being the maximal ones. Only in one (12.5%) patient did the postprandial levels of triglyceride fall below the basal level, with the 3 hour level also being below the basal level (See Appendix-II). These changes were not found to be statistically significant.

Changes in LDL/HDL ratio

The LDL/HDL ratio had a fasting mean of 4.18 for group B patients. It exhibited considerable constancy in the postprandial phase, varying less than 0.2 in either direction (Table 5). No discernible trend was noticed in its variation in individual patients, except that the ratio of least magnitude (1.8) was seen in the youngest patient in the group, an 11 year old boy (See Appendix-II).

CHANGES IN GROUP C

Changes in Serum Total Cholesterol (STC)

The mean fasting STC level in group C patients, at 295.02 ± 76.88 mg/dl, was the highest amongst all the four disease groups studied (Table 1). It demonstrated a sustained rising trend in all the three postprandial values, rising to 321.63 ± 80.12 mg/dl, at 3 hours, an increase of 9.01 percent over the fasting value (Table 16).

Two types of subgroups were formed on the basis of the changes in STC levels found at 1 hour after ingestion of the test diet. Thus, there were 2 patients in the type C-I subgroup, with a greater than 5% rise in STC over the basal value (Table 15). Their mean fasting STC level was 253.5 ± 65.76 mg/dl and the mean 1 hour STC level was 279 ± 66.46 mg/dl. The difference was statistically insignificant. In the type C-II subgroup, there were 7 patients, with a mean fasting STC of 306.89 ± 80.13 mg/dl and a mean 1 hour STC of 312.53 ± 87.7 mg/dl. This

difference was statistically insignificant on applying the student 't' test.

TABLE 15 : Showing the two different types of responses in 1 hour STC in group C after administration of single high cholesterol test diet and their statistical significance on application of paired 't' test. (Mean \pm SD, mg/dl).

Category (n)	Fasting	After 1 hour	p value
C-I (2)	253.50 \pm 65.76	279.00 \pm 66.46	7 0.1
C-II (7)	306.89 \pm 80.13	312.53 \pm 87.72	7 0.5

Changes in HDL Cholesterol

In contrast to the other disease groups, group C patients demonstrated the greatest differences between fasting and postprandial serum HDL-c levels (Table 2). The mean fasting HDL level was 53.44 \pm 19.9 mg/dl, and it displayed a steady rise to a level of 74.42 \pm 38.75 mg/dl 3 hours after ingestion of the test diet, a rise of 39.25% over the fasting level (Table 16). This difference, however, was not found to be statistically significant on applying the student 't' test.

All nine subjects in the group (100%) displayed a rise in the first hour HDL levels over their basal levels. After 2 hours, 5 out of 9 patients (55.6%) demonstrated a further rise in their HDL levels, 2 patients (22.2%) showed no change from the previous level, and 2 patients (22.2%) showed a slight fall in HDL concentration from the previous 1 hour value. However, at 3 hour

8(88.89%) of the 9 patients, had further increase in HDL levels from the previous levels, only in 1 patient was there a slight fall from the 2 hour value. The 3 hour levels were greater than the fasting levels in all 9 patients (See Appendix - III). None of the changes was seen to be statistically significant. The variations at the two hour interval therefore were transient in almost all the patients.

Changes in LDL Cholesterol

The mean fasting LDL-c concentration was 144.95 ± 36.81 mg/dl in group C patients (Table 3), and in contrast to the STC and HDL-c concentrations, it showed a steadily declining level in the postprandial phase, with the 3 hour level of 116.68 ± 32.67 mg/dl being the lowest, representing a fall of 18.12 percent from the fasting level (Table 16). Only in 2 (22.2%) patients did the changes in LDL-c concentration appear to run contrary to the norm for this lipoprotein, and consequently they had 3 hour LDL levels that were slightly higher than their basal levels. None of the changes described above were statistically significant on applying the student 't' test.

Changes in Serum Triolyceride (STG)

Hypertriglyceridemia was evident from the fasting as well as postprandial mean STG concentrations

of patients in this group (Table 4). The mean fasting STG level was 482.97 ± 173.36 mg/dl, which showed a sustained rise till the 3 hour interval to a level of 642.8 ± 250.75 mg/dl, an increase of 33.09 percent over the basal level (Table 16). None of the increases, however, was statistically significant. All nine patients in this group without any exception showed a gradual and sustained rise in their STG concentrations at every hour after the test diet, attaining their highest values at the 3 hour.

TABLE 16 : Showing percentage variance (from the fasting level) of the postprandial levels of different lipid lipoprotein fractions in subjects of group C.

Type of lipids	Percentage change after		
	1 hour	2 hour	3 hour
STC	+ 3.39	+ 4.70	+ 9.01
HDL	+ 18.71	+ 28.77	+ 39.25
LDL	- 9.23	- 17.47	- 18.12
STG	+ 13.96	+ 25.45	+ 33.09

Changes in LDL/HDL Ratio

The mean LDL/HDL ratio showed a gradual stepwise decrease from the basal to the 3 hour interval (Table 5). None of these changes was found to be statistically significant on applying the student 't' test. In 8 out of 9 patients (88.9%), the LDL/HDL ratio was lower than fasting value, at 3 hours. In only one patient (11.1%) was it marginally greater at 3 hours than at

fasting. These differences however, were not statistically significant. No definite trend was discernible regarding the changes seen at one and two hours after ingestion of the test diet.

CHANGES IN GROUP D

The mean fasting STC level in group D patients was 185.99 ± 50.2 mg/dl (Table 1). This rose to 203.26 ± 52.8 mg/dl, 1 hour after ingestion of the test diet, a rise of 9.28 percent over the basal level (Table 18). It declined again at 2 hours, followed by a slight rise at 3 hours. Thus all the three postprandial values were higher than the fasting value, with the level being highest at 1 hour after ingestion of the test diet.

Since none of the patients exhibited a decline of more than 5% from the fasting levels, only two subgroups were formed on the basis of STC changes at 1 hour. There were six patients in the D-I subgroup (Table 17) whose mean fasting STC was 176.15 ± 53.14 mg/dl, and the mean 1 hour value was 207.15 ± 59.16 mg/dl. The difference was statistically not significant ($p > 0.05$). In the type D-II subgroup, there were four patients, with a mean fasting STC of 200.76 ± 48.7 mg/dl, and a mean 1 hour STC of 197.41 ± 47.52 mg/dl. This difference was statistically not significant on applying the student 't' test. Also the difference between the two subgroups was statistically not significant on applying the student 't' test.

TABLE 17 : Showing the two different types of responses in 1 hour STC in group D after administration of single high cholesterol test diet and their statistical significance on application of paired 't' test (Mean \pm SD, mg/dl).

Category (n)	Fasting	After 1 hour	p value
D-I (6)	176.15 \pm 53.14	207.15 \pm 59.16	7 0.1
D-II (4)	200.76 \pm 48.69	197.41 \pm 47.52	7 0.5

Changes in HDL Cholesterol

The mean fasting HDL cholesterol level was 38.33 \pm 11.09 mg/dl in these patients (Table 2) and was almost unchanged after 1 hour, showed a slight decline at 2 hour and again was almost unchanged at 3 hours; the 3 hour level of 35.97 \pm 8.44 mg/dl representing a fall of 6.15 percent from the fasting level. None of these changes was seen to be statistically significant on applying student 't' test.

Four out of ten patients (40%) had a lower HDL-c level at 3 hours than at fasting, while six (60%) had higher HDL-c levels at 3 hours than at fasting. The difference was statistically not significant (p 70.05).

Changes in LDL Cholesterol

The mean fasting LDL cholesterol was 129.59 \pm 37.61 mg/dl in group D patients (Table 3). This showed a rise of 9.27 percent at 1 hour after ingestion of the test diet (Table 18) followed by a fall at 2 hours, with only a very slight further decrease at 3 hours. None of these

changes were found to be statistically significant on applying the student 't' test. All the three postprandial values were higher than the fasting value, with the 1 hour value being the highest at 141.61 ± 40.22 mg/dl.

Six out of ten patients (60%) showed a rise in LDL-c levels at 1 hour, while 4(40%) patients had a lower 1 hour level of LDL-c than the fasting level. The rise in case of 6 patients was statistically not significant ($p > 0.05$), the decrease seen at 1 hour in the four remaining patients was also statistically insignificant.

Changes in Serum Triglyceride (STG)

The mean fasting STG level in group D patients was 90.39 ± 24.74 mg/dl (Table 4). In the postprandial phase, a regular rise in the STG level was noticed at every hour, with the maximal value being reached at 3 hours after ingestion of test diet. The difference was statistically insignificant.

It was especially noted that the percentage rise in STG over the fasting level was 29.04 percent at 1 hour, 42.46 percent at 2 hours and 55.34 percent at 3 hour (Table 18). This magnitude of rise in STG was the greatest amongst all the four disease groups studied, not just in STG, but in any other lipoprotein fraction as well. Thus patients of COPD displayed a sharp rise in STG levels in the postprandial phase from the first to the third hour. The difference was found to be statistically not significant ($p > 0.05$).

TABLE 18: Showing percentage variance (from the fasting level) of the postprandial levels of different lipid lipoprotein fractions in subject of group D.

Type of lipids	Percentage change after		
	1 hour	2 hour	3 hour
STC	+ 9.28	+ 3.92	+ 5.00
HDL	- 0.05	- 6.86	- 6.15
LDL	+ 9.27	+ 1.70	+ 1.26
STG	+ 29.04	+ 42.46	+ 55.34

In all the ten patients, the 3 hour levels were considerably above their fasting STG levels, with the 3 hour STG concentration being the highest in eight (80%) patients, while two (20%) patients had their highest STG concentrations at 2 hours.

Changes in LDL/HDL Ratio

The mean fasting ratio was 3.45 for the group. There was a small but sustained increase in the ratio upto the 2 hour level, with the 3 hour value being almost identical to the 2 hour value (Table 5). These changes were found to be insignificant on statistical analysis.

As compared to their fasting level of the ratios, half the patients demonstrated a fall in the value at 3 hours, while the other half demonstrated a rise in the value of the ratio at 3 hours. These differences were found to be statistically not significant ($p > 0.05$) on applying the student 't' test. No significant discernible trend was noticed regarding the changes seen at 1 hour and 2 hour.

D I S C U S S I O N

D I S C U S S I O NCHANGE IN GROUP AChanges in Serum Total Cholesterol (STC)

The fasting STC level in group A subjects was 194.51 ± 53.07 mg/dl. There was a fall in this level 1 hour after ingestion of the test diet, and then a rising trend was noticed in the second and third hours.

On splitting the subjects into the two subgroups of IDDM and NIDDM, however, a marked difference was noticed in the fasting as well as all the postprandial values between the two, with the NIDDM patients having a markedly higher fasting STC concentration of 236.66 ± 45.1 mg/dl, in contrast to the 158.38 ± 25.22 mg/dl of IDDM patients, a difference that was statistically significant ($p < 0.05$). One hour after ingestion of the test diet, this decreased to 219.66 ± 29.16 mg/dl, a fall of 7.18 percent from the basal values; there was a progressive rising trend in the second and third hour values.

In marked contrast to this was the trend of STC in the IDDM subgroup, wherein the 1 hour postprandial value rose above the fasting level, and continued to rise at 2 and 3 hours, with the highest value being reached at 3 hours, to 175.95 ± 14.69 mg/dl, a rise of 11.09 percent over the fasting level. The difference between the two subgroups at 1 hour was statistically highly significant ($p < 0.02$), and the differences at 2 and 3 hours were also statistically significant ($p < 0.05$).

Thus on the basis of post prandial response the diabetic population can be divided into three groups. Almost half the population (6 patients) showed a fall in STC concentration 1 hour after feeding, an equal proportion (6 patients) showed a rise in STC at 1 hour, and one patient showed no change from the fasting level at 1 hour.

In the past also, Nikkila et al (1962) and Havel (1957) have reported a fall in STC concentration after feeding. The explanation for this fall could be related to the suppression of LDL receptors after overnight fasting (Medical Clinics of North America Vol 66 No. 2, March, 1982, p. 344). When a high cholesterol load is given, LDL receptors are stimulated by some as yet undefined hormonal or neurogenic reflexes, in anticipation of the cholesterol load that will enter the circulation. Consequently, a large amount of LDL from the intravascular compartment shifts intracellularly, resulting in an acute fall in serum LDL and STC levels after 1 hour. The cholesterol levels slowly increase thereafter as a result of the absorbed cholesterol entering the circulation, and the reversal of movement of LDL that had entered the tissues earlier.

By the same reasoning, the rise in serum cholesterol in other patients could be explained by some inherent biochemical block in the above mentioned mechanism, in anticipating and assimilating the cholesterol load. The fact that IDDM patients were more prone to display this kind of behaviour suggests that aetiological factors of

IDDM play a dominant role in disruption of the above mentioned mechanism. But this is not exclusively the case, as shown by the fact that there were two patients in the IDDM subgroup, who showed a fall in STC, after 1 hour, and also there being two patients in the NIDDM subgroup who showed a rise in the 1 hour STC concentration.

Changes in HDL Cholesterol

The fasting and postprandial levels of HDL-c were within normal range in both IDDM and NIDDM patients and showed very little variation in the postprandial phase. Nor were there any marked differences between the two subgroups. Age, sex and smoking did not affect the HDL profile in any way.

Changes in LDL Cholesterol

A mean fasting LDL cholesterol concentration of 119.90 ± 42.71 mg/dl was noted in the group as a whole, with a fall in the 1 hour value to 110.83 ± 24.73 mg/dl followed by a slight rise at 2 and 3 hour intervals. The trend in LDL thus mirrors exactly the trend seen in STC concentrations. The same holds true for the trends of IDDM and NIDDM subgroups. Marked differences were observed in all the respective values, between the two subgroups, with NIDDM patients having considerably higher LDL-c concentrations. Except the third hour, all these differences were statistically significant ($p < 0.05$), with that at two hour being statistically highly significant ($p < 0.02$). Intracellular

movement of LDL in the immediate postprandial phase seems to be the explanation for this, as narrated earlier for STG. No age, sex or diabetic-control related differences was observed.

Changes in Serum Triglycerides (STG)

The fasting levels of STG in IDDM and NIDDM were 135.17 ± 27.42 and 212.73 ± 78.07 mg/dl respectively. Both IDDM and NIDDM patients showed a gradual and sustained rise in STG levels after ingestion of test diet, with the highest values being reached at 3 hours in both groups - the difference at 3 hours between the two groups being statistically significant. Brown et al (1961) and Angervall (1964) reported peak STG levels four hours after feeding in healthy subjects.

Treatment of diabetics with insulin results in decreased levels of triglyceride and VLDL, though the levels are still higher than in normal persons, as documented by Lewis et al (1972). The reason for this is the enhancement of lipoprotein lipase activity by the exogenously administered insulin. The fact that all the IDDM patients in our study were well controlled with insulin regimens could account for the finding of comparatively lower triglyceride concentrations in this subgroup.

Changes in VLDL

Changes in VLDL were exactly similar to those of STG.

CHANGES IN GROUP BChanges in STC

The mean fasting STC was 159.32 ± 48.34 mg/dl, the lowest amongst all the four disease groups. There was, however, a pronounced rise of 13.55% after 1 hour of diet ingestion, with marginally lower subsequent values - all postprandial values being above the fasting one. What was noteworthy was that all the eight patients in this group showed a rise in STC levels at the first hour. No studies as yet have been conducted on the postprandial lipid profile in these patients. Stigendahl et al (1984) have stated that there is reduced synthesis of endogenous cholesterol in cirrhotics. This could explain the low fasting STC levels in our patients, whereas the marked rise in STC levels after ingestion of exogenous cholesterol can be attributed to decreased clearance from plasma due to hepatic lipase inhibition, a finding reported by Schaefer et al (1985). Also decreased intake due to the marked anorexia in these patients could be another cause that requires quantification.

Changes in HDL Cholesterol

The HDL cholesterol levels increased after 1 hour but thereafter displayed only very marginal changes. The slight decrease shown by some patients at 2 hours appeared to be a transient phenomenon, as the values rose again at 3 hours; the two patients in whom the 3 hour level showed

a downward trend happened to be those whose 1 hour value of HDL-c had also stayed unchanged from the fasting level. We recommend further studies to explain the significance of the above finding in our study, as no explanation is forthcoming at present.

Changes in LDL Cholesterol

Five out of eight patients showed a rise in LDL-c at 1 hour, and all of these except one continued to show further rise at 3 hour.

In contrast, the remaining three patients who had a fall in LDL-c at 1 hour, in all these three, the downward trend continued till the third hour also, with the 3 hour values dropping below the basal level.

Thus two distinct trends could be appreciated, and we recommended further studies on larger groups of patients to elaborate further the cause of the same. Differences in hepatic LDL receptor activity could be one explanation.

Changes in Serum Triglycerides (STG)

Seven of the eight patients showed a gradual postprandial rise in STG, peaking at 3 hours. Schaefer et al (1985) have also reported increased levels of triglycerides, chylomicrons and VLDL in patients of primary biliary cirrhosis, and have attributed these abnormalities to hepatic lipase inhibition and altered cholesterol esterification.

Changes in VLDL

These were exactly similar to those in STC.

CHANGES IN GROUP C

Changes in STC

The highest fasting (295.02 ± 76.83 mg/dl) as well as postprandial STC levels were observed in this group of patients, although the postprandial rise in STC was only slight (maximum 9% at 3 hours). Hyperlipidaemia is a well known feature of chronic renal insufficiency. Cholesterol ester turnover has been found to be raised together with triglyceride turnover in patients with the nephrotic syndrome (Mckenzie et al, 1968), and a possible relationship between cholesterol ester turnover and lipoprotein transport has emerged from the study of Nestel and associates (1968, 1970).

Our findings of only a very slight rise in STC in the postprandial phase finds support in the view of Kayden et al (1963), that the composition of plasma cholesterol esters is only minimally affected by a single meal of a specific fat, but is readily influenced thereafter.

Changes in HDL Cholesterol

This was the only group in which the HDLC showed a marked rise from the basal (53.44 ± 19.9 mg/dl) to the postprandial levels, rising to 74.42 ± 38.75 mg/dl at 3 hour, a rise of almost 40 percent over the fasting level. Since eight out of nine patients were of nephrotic syndrome,

understandably, the hyperlipidaemia associated with this condition has overtly influenced the overall mean HDL-c levels. Joven and Villabona et al (1990) stated that overproduction of lipoproteins containing apoprotein B is the principal cause of hyperlipidaemia in these patients, but Karadi and Romics et al (1989) found that serum lipoprotein (a) levels may be increased. The lone patient of CRF in this group had fasting and 3 hour HDL-c levels of 18 and 20 mg/dl respectively, much below the group mean. This conforms to the established finding of low HDL levels in CRF (Lewis et al, 1966, Rapoport and Aviram et al, 1978; Goldberg and Harter et al, 1983), although the reasons had not been defined. But recent studies show that low serum HDL concentrations in patients with CRF are related to decreases in the synthetic rate of apo AI/HDL (Martin Fuh, C-Ming Lee et al, 1990).

Changes in LDL Cholesterol

The fasting level of 144.95 ± 36.81 , decreased gradually to 118.68 ± 32.67 mg/dl after 3 hours. The marked progressive rise of HDL-c levels could be held responsible for affecting the derivation of LDL cholesterol values.

Changes in Serum Triglycerides (STG)

Hypertriglyceridaemia is a characteristic feature of nephrotic syndrome, as is apparent from the markedly high fasting and postprandial values, rising to 642.8 ± 250.75 mg/dl at 3 hours, an increase of 33 percent over

the fasting value. This increase however, was not statistically significant due to the large standard deviation and small sample size. We recommend further studies with larger population groups to properly quantify the changes.

Murase et al (1975) provided evidence of a factor in uraemic plasma which inhibits lipoprotein lipase activity. This results in decreased clearance of triglycerides from plasma.

Changes in VLDL

Changes in VLDL are exactly similar to changes in STG.

CHANGES IN GROUP D

Changes in STC

Both the mean fasting and postprandial levels of STC were within normal range as established by Lipid Research Clinics with the post prandial levels showing only a minor and statistically insignificant rise. Studies in humans and primates have demonstrated that respiratory infections lead to lowered plasma cholesterol levels (Kerttula and Weber et al, 1988; Fiser and Denniston et al, 1972), since repeated respiratory infections are a feature of COPD, this could be one reason for the absence of any significant rise in STC levels in the postprandial phase.

Previously also, respiratory disease mortality has shown inverse association with cholesterol levels

(Kozarevic and McGee et al, 1981; Kagan and McGee et al, 1981; Neaton and Blackburn et al, in press). However, Smith and Shipley et al (1992), while confirming that such a relationship exists, argue that mortality studies do not allow for examination of the temporal relationship between the development of respiratory morbidity and plasma cholesterol level.

Changes in HDL Cholesterol

The mean fasting HDL cholesterol level was 38.33 ± 11.09 mg/dl which was almost unchanged for 2 hours after ingestion of the test diet, showing a slight decline at 3 hours to 35.97 mg/dl. Thus, there was no significant change in the HDL cholesterol level.

Changes in LDL Cholesterol

The mean fasting LDL-c level was 129.59 ± 37.61 mg/dl. This showed a small rise of 9.27 percent at 1 hour, followed by very slight decreases at 2 and 3 hours. None of these changes were significant and no distinct trends could be identified.

Changes in STG

The most notable finding that emerged from our study of COPD patients was the sustained and sharp increase in STG concentration in the post prandial phase, while the fasting STG levels were within normal limits

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(90.39 \pm 24.74 mg/dl). The 1st, 2nd and 3rd hour mean levels showed a rise of 29, 42 and 55 percent respectively, over the fasting level.

This is the greatest magnitude of rise in STG in the postprandial phase seen in the four disease groups in this study. Even though the rise was not statistically significant. We believe that the relatively large standard deviation along with the small sample size could be responsible for the same, and therefore strongly urge that further studies with larger sample groups be carried out to elucidate the qualitative and quantitative significance of these changes.

SUMMARY & CONCLUSION

S U M M A R Y A N D C O N C L U S I O N S

In the present work 13 male and female patients of endocrine and metabolic disease, 8 male and female patients of chronic liver disease, 9 male and female patients of chronic renal insufficiency and 10 male patients of chronic obstructive pulmonary disease were studied to see the response of an individual to stress of single high cholesterol test load in diseased state. Following conclusions were drawn from the present study.

1. There was a fall in STC concentration in group A patients 1 hour after ingestion of the cholesterol test diet, and then a rising trend was noticeable in the second and third hours; and this fall and rise trend was especially marked in the NIDDM subgroup of group A patients,,with 1 & 3 postprandial levels below the fasting level.
2. In marked contrast, patients in IDDM subgroup of group A showed a trend wherein the STC concentration 1 hour after ingestion of test diet, rose above the fasting level, and continued to rise at 2 and 3 hours, with the highest value being reached at 3 hours after the ingestion of test diet.
3. The fasting serum total cholesterol in the NIDDM subgroup of group A was found to be statistically significantly higher than the fasting serum total cholesterol in the IDDM subgroup ($p < 0.05$).

4. The STC concentration 1 hour after ingestion of the test diet showed a difference between the IDDM and NIDDM subgroups of group A, which was of even greater statistical significance ($p < 0.02$), than at fasting.
5. The 2 hour and 3 hour differences in STC concentration between the two subgroups were also of statistical significance ($p < 0.05$).
6. The trend in low density lipoprotein concentrations was found to mirror exactly the trend seen in STC concentrations, with the same holding true for the trends of IDDM and NIDDM subgroups.
7. In the NIDDM subgroup, the fasting 1, 2 and 3 hour LDL concentrations were considerably higher than those in the IDDM subgroup. Except for the third hour, all these differences were found to be statistically significant ($p < 0.05$).
8. Both IDDM and NIDDM patients showed a gradual and sustained rise in serum triglyceride levels after ingestion of the test diet, with the highest values being reached at 3 hours in both subgroups, and the difference in STC at 3 hours between the two subgroups being statistically significant ($p < 0.05$).
9. The mean fasting STC was lowest in group B patients amongst all the four disease groups studied. However, all eight patients in this group showed a rise in STC level at 1 hour.

10. Two distinct trends were noticed in the changes in LDL concentration in group B patients. Majority of the patients showed a rise in LDL levels at 1 hour and continued to show a further rise at 3 hours. A minority of the patients, however, showed a fall in LDL at 1 hour, and continued to show a further fall at 3 hours. These differences, however, were not statistically significant.
11. Highest fasting as well as postprandial levels of STC were observed in group C, although the postprandial rise in STC was slight (Maximum 9% at 3 hours).
12. Group C was the only group in which HDL-c showed a marked rise from the basal to the postprandial levels, rising almost 40 percent over the fasting levels, 3 hours after ingestion of the test diet. Whereas in group A, B and D patients, HDL-c had shown minimal variability from fasting to postprandial phase.
13. The HDL-c levels in the case of nephrotic syndrome patients were markedly higher than in case of CRF patients, and also exhibited greater variation in the fasting and postprandial phase.
14. The LDL cholesterol concentration in group C patients showed a steady decline from fasting to the postprandial phase, reaching the lowest concentration 3 hours after ingestion of high cholesterol test diet.

15. Highest fasting and postprandial levels of serum triglyceride were observed in Group C patients of nephrotic syndrome, with the 3 hour mean value being 33 percent higher than the mean fasting value. The difference was not statistically significant, hence further studies with larger groups were recommended to properly quantify the changes.
16. Both the mean fasting and postprandial levels of STC were within normal range in Group D patients of COPD, with the postprandial levels showing only a minor and statistically insignificant rise over the fasting level.
17. The mean fasting HDL cholesterol level in COPD patients (Group D) was almost unchanged for 2 hours after ingestion of the test diet, showing a slight decline at 3 hours. Whereas the LDL cholesterol level in this group showed a small rise at 1 hour followed by very slight decreases at 2 and 3 hours. None of these changes was significant and factors like alcohol, age, smoking and secondary infection did not have any significant effect upon any of the lipid parameters studied.
18. In patients of group D (Chronic obstructive pulmonary disease) the 1st, 2nd and 3rd hour postprandial mean

serum triglyceride (STG) levels showed a rise of 29, 42 and 55 percent respectively over the fasting level, which was the greatest magnitude of rise in STG following ingestion of the test diet amongst the four disease groups included in this study. As no such comparative prior studies have been done on COPD patients, it was strongly urged that further studies with larger sample groups be carried out to elucidate the quantitative and qualitative significance of these changes.

B I B L I O G R A P H Y

B I B L I O G R A P H Y

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A P P E N D I X

MASTER CHARTAPPENDIX - I

General characteristics of the patients. (Group A)

Sl. No.	Name	Age/ sex	Wt. (kgs.)	Height (cms)	Diag- nosis	Smoking	Alcohol
1.	S. Lal	28/M	48	140	IDDM	NO	NO
2.	R. Kunwar	27/F	50	151	IDDM	NO	NO
3.	M. Chand	18/M	41.5	142.5	IDDM	NO	NO
4.	Madhvi	35/F	40	135	IDDM	NO	NO
5.	R. Sewak	26/M	51	160	IDDM	YES	NO
6.	K. Pd.	36/M	53	158	IDDM	YES	NO
7.	Hari Ram	30/M	52	163	IDDM	NO	YES
8.	K. Narain	40/M	66	155.5	NIDDM	NO	NO
9.	VK Sahu	67/M	64	160	NIDDM	NO	NO
10.	B. Das	46/M	56	157	NIDDM	YES	NO
11.	S. Sharma	50/F	56	160	NIDDM	NO	NO
12.	S. Lal	47/M	42	152.5	NIDDM	YES	YES
13.	M. Singh	50/M	58	160	NIDDM	YES	NO

APPENDIX- IIGeneral characteristics of patients of
group B

Sl. No.	Name	Age/ Sex	Wt. (kgs.)	Height (cms)	Diag- nosis	Smoking	Alcohol
1.	Bare Lal	60/M	56	157.5	Cirrhosis	YES	YES
2.	A. Mazid	60/M	50	162.5	-do-	Yes	NO
3.	P. Devi	35/F	43	150	-do-	NO	NO
4.	Sur Sen	45/M	50	150	Cirrhosis with grade I bleed	YES	NO
5.	Isue	11/M	28	110	Cirrhosis Koch's lung	NO	NO
6.	Raja Bai	67/F	46	167	Cirrhosis	NO	NO
7.	Raj Rani	55/F	50	152.5	-do-	NO	NO
8.	K. Ram	58/M	70	162.5	-do-	Yes	NO

APPENDIX - III

General characteristics of patients of group C.

Sl. No.	Name	Age/Sex	Wt. (kgs.)	Height (cms)	Diagnosis	Smoking	Alcohol
1.	Shakti	25/F	51	145	Nephrotic syndrome	NO	NO
2.	P. Lal	42/M	49	150	-do-	NO	NO
3.	B. Mohd.	50/M	54	152	-do-	Yes	NO
4.	Hari Singh	28/M	40	155	CRF, Syst. Hypertension	Yes	NO
5.	S. Kumar	16/M	37.2	150	Nephrotic syndrome	NO	NO
6.	Kailash	30/M	57	162.5	-do-	NO	NO
7.	A. Pd.	56/M	60	164	NS, Syst. hypertension	NO	NO
8.	R. Kumar	23/M	50	157	NS + Koch's lungs	NO	NO
9.	Dugola	50/F	55	150	Nephrotic syndrome.	NO	NO

APPENDIX - IV

General characteristics of patients of group D.

Sl. No.	Name	Age/Sex	Wt. (kgs.)	Height (cms.)	Diagnosis	Smoking	Alcohol
1.	G. Das	56/M	52	170	COPD	YES	NO
2.	Tijuram	70/M	54	145	COPD	YES	NO
3.	M. Singh	58/M	60	155	COPD C sec. infection	YES	NO
4.	Ram Das	53/M	49.5	162.5	COPD	YES	NO
5.	Raghunath	60/M	53.5	152.5	COPD	YES	Occas.
6.	Paloo	80/M	54	160	COPD	Yes (stopped)	NO
7.	Babulal	55/M	57	167.5	COPD C Cor pulmonale	YES	NO
8.	S. Sunder	40/M	52	150	-do-	YES (stopped)	NO
9.	A. Rashid	60/M	54	162.5	Bronchial Asthma	Yes (stopped)	Yes (Stopped)
10.	Babloo	60/M	48	170	COPD, Koch's Lung, Rt. pleural effusion	YES	NO

MASTER CHART
Values of lipid lipoproteins.

Sl. No.	STC			STG			HDL					
	Fasting	1 hour	2 hours	3 hours	Fasting	1 hour	2 hours	3 hours	Fasting/1 hour	2 hour	3 hour	
GROUPS A												
1.	187.50	181.2	175.0	187.5	118.9	121.7	138.7	161.3	37.5	35.0	33.8	32.5
2.	152.2	163.0	173.9	162.5	146.7	180.0	226.7	244.7	39.5	37.5	40.0	45.3
3.	160.2	187.5	181.2	187.5	79.8	114.9	127.7	146.8	33.0	33.5	35.0	34.0
4.	193.8	162.5	162.5	181.2	146.8	159.6	191.5	244.6	33.8	37.5	35.0	37.5
5.	125.0	135.0	140.0	150.0	150.0	160.0	200.0	220.0	33.0	36.0	30.0	27.0
6.	155.0	165.0	172.0	188.0	160.0	160.0	152.0	200.0	48.0	47.0	49.0	43.0
7.	135.0	145.0	150.0	175.0	144.0	120.0	138.0	120.0	53.0	41.5	50.0	50.0
8.	180.0	180.0	190.0	185.0	95.4	98.9	170.4	238.6	25.0	21.2	23.8	21.2
9.	225.0	230.0	235.0	190.0	256.0	321.0	301.0	235.0	41.6	41.8	40.2	30.5
10.	309.0	268.0	268.0	262.0	331.0	425.0	330.0	350.0	57.0	59.0	59.0	59.0
11.	261.0	220.0	243.0	214.0	188.0	195.0	200.0	244.0	36.7	36.7	39.0	50.0
12.	205.0	215.0	214.0	205.0	208.0	220.0	220.0	274.0	43.0	44.5	44.0	41.6
13.	240.0	205.0	200.0	260.0	198.0	214.0	180.0	250.0	28.5	47.2	39.0	44.0
GROUP B												
1.	138.75	145.0	143.75	138.75	100.0	90.0	120.0	120.0	16.66	26.66	23.66	23.66
2.	125.0	131.25	128.85	125.0	178.5	231.57	231.57	240.39	20.0	21.25	23.0	18.76
3.	135.0	182.5	150.0	156.25	76.59	57.44	70.21	70.21	15.0	16.25	12.5	13.75
4.	135.0	150.0	145.0	156.25	75.45	89.09	95.45	98.86	19.0	20.0	19.0	23.0
5.	150.0	165.62	178.0	181.25	189.47	228.94	230.47	259.5	40.0	57.5	63.5	60.0
6.	243.75	250.0	256.25	260.0	189.47	200.0	231.57	278.38	40.0	43.75	35.0	40.0
7.	228.12	312.5	290.62	290.62	270.0	339.47	339.47	342.00	45.0	56.66	43.33	49.66
8.	119.0	130.5	132.5	130.5	89.47	110.52	89.47	100.9	26.25	26.25	34.69	26.25

GROUP C

1.	406.25	425.0	437.5	437.5	702.12	868.08	931.91	944.68	60.00	97.50	128.75	130.00
2.	373.0	273.0	262.5	297.5	510.63	631.91	682.97	765.95	55.00	61.50	62.00	69.00
3.	359.25	365.0	350.0	269.25	638.2	695.74	874.46	893.46	80.50	90.00	90.00	112.75
4.	186.5	181.25	186.5	190.75	148.0	159.0	176.0	187.0	18.00	20.00	22.40	20.00
5.	378.25	394.0	408.0	416.0	624.08	787.08	842.41	873.18	80.00	106.5	120.5	124.00
6.	310.0	310.0	323.5	341.5	538.66	540.66	596.33	626.66	50.50	52.00	51.50	56.00
7.	207.0	232.0	230.0	256.0	332.33	360.33	366.66	428.33	58.00	60.00	60.00	65.50
8.	235.0	239.5	256.25	256.25	386.08	407.51	452.9	496.33	42.30	44.10	42.30	48.00
9.	300.0	326.0	332.0	330.0	466.66	503.33	529.66	569.66	36.74	39.37	42.00	44.60

GROUP D

1.	262.5	300.0	268.75	256.25	127.65	178.72	191.48	178.72	62.50	46.00	37.50	32.50
2.	119.56	130.43	125.00	130.43	73.33	73.33	80.00	93.33	26.93	26.93	19.76	22.50
3.	155.00	150.00	160.00	160.00	95.45	109.09	132.95	144.35	35.00	37.50	40.00	42.50
4.	156.25	187.50	181.25	187.50	79.78	102.12	114.85	108.51	22.50	25.00	22.50	25.00
5.	156.25	187.50	181.25	187.50	79.78	114.79	127.65	146.80	33.00	33.50	35.00	34.00
6.	250.00	239.13	250.00	228.26	106.66	126.66	143.33	180.00	45.34	44.18	41.86	44.18
7.	145.00	187.50	156.25	160.00	67.02	102.12	108.51	121.32	40.00	35.00	44.00	44.00
8.	217.39	250.00	206.52	228.26	93.33	146.66	163.33	166.66	41.86	47.67	48.83	47.67
9.	163.04	163.04	141.30	152.17	53.33	53.33	53.33	66.66	33.70	34.88	32.55	34.88
10.	235.00	237.50	262.50	262.50	127.65	159.57	172.34	197.87	42.50	42.50	35.00	32.50

Sl. No.	LDL			VLDL			LDL/HDL					
	Fasting	1 hour	2 hour	3 hour	Fasting	1 hour	2 hour	3 hour	Fasting	1 hour	2hr	3hr
GROUP A												
1.	126.40	121.90	113.50	122.70	23.78	24.34	27.74	32.26	3.40	3.50	3.40	3.80
2.	83.30	89.50	88.60	68.20	29.34	36.00	45.34	48.94	2.10	2.40	2.20	1.50
3.	111.30	131.00	120.70	124.10	15.96	22.98	25.54	29.36	3.40	3.90	3.40	3.60
4.	130.60	93.10	89.20	94.80	29.36	31.92	38.30	48.92	3.90	2.50	2.50	2.50
5.	62.00	67.00	70.00	79.00	30.00	32.00	40.00	44.00	1.90	1.90	2.30	2.90
6.	75.00	86.00	92.60	105.00	32.00	32.00	30.40	40.00	1.60	1.80	1.90	2.40
7.	53.20	79.50	72.40	101.00	28.80	24.00	27.60	24.00	1.00	1.90	1.40	2.00
8.	135.90	139.00	132.20	126.00	19.08	19.78	34.08	47.72	5.40	6.30	5.60	5.90
9.	132.20	124.00	134.60	112.50	51.20	64.20	60.20	43.00	3.20	3.00	3.40	3.70
10.	185.80	124.00	143.00	133.00	66.20	85.00	66.00	70.00	3.30	3.10	2.40	2.20
11.	186.70	144.30	164.00	115.20	37.60	39.00	40.00	48.80	5.10	3.90	4.02	2.30
12.	120.40	126.50	126.00	108.60	141.60	44.00	44.00	54.00	2.80	2.80	2.90	2.60
13.	155.90	115.00	125.00	166.00	39.60	42.80	36.00	50.00	3.50	2.40	3.20	3.80
GROUP B												
1.	102.09	100.34	96.09	91.09	20.00	18.00	24.00	24.00	6.12	3.76	4.06	3.84
2.	69.30	63.69	61.94	58.18	35.70	46.31	46.31	48.07	3.46	2.99	2.69	3.10
3.	104.69	134.77	123.46	128.46	15.31	11.48	14.04	14.04	6.89	8.29	9.87	9.34
4.	100.91	112.91	106.91	113.48	15.09	17.81	19.09	19.77	5.31	5.61	5.62	4.93
5.	72.11	62.34	68.41	69.35	37.89	45.78	46.09	51.50	1.80	1.08	1.07	1.15
6.	165.86	166.25	174.94	164.83	37.89	40.00	46.31	55.67	4.14	3.80	4.99	4.12
7.	129.12	187.95	179.40	172.56	54.00	67.89	67.89	68.40	2.86	3.31	4.14	3.47
XXXXXXXXXXXXXXXXXXXXXXXXXXXX												
8.	74.86	82.15	79.92	84.67	17.89	22.10	17.89	20.18	2.85	3.12	2.30	3.20

GROUP C

1.	205.59	153.90	122.55	118.57	140.42	173.60	186.20	188.93	3.42	1.57	0.95	0.91
2.	115.68	85.12	63.91	75.31	102.12	126.38	136.59	153.19	2.10	1.38	1.03	1.09
3.	151.11	135.86	85.36	78.06	127.64	139.14	174.89	178.69	1.88	1.51	0.95	0.70
4.	138.90	129.45	128.90	133.35	129.60	31.80	35.20	37.40	7.72	6.47	5.75	6.66
5.	173.43	130.08	119.02	117.37	124.82	157.42	163.48	174.63	2.17	1.22	0.99	0.95
6.	151.77	149.87	152.74	160.17	107.73	108.13	119.26	125.33	3.00	2.88	2.96	2.86
7.	82.54	99.94	96.67	104.84	66.46	72.06	73.33	85.66	1.42	1.66	1.61	1.60
8.	115.49	113.90	123.37	108.99	77.21	81.25	90.58	99.26	2.70	2.58	2.90	2.27
9.	169.93	185.97	184.07	171.47	93.33	100.66	105.93	113.93	4.62	4.72	4.38	3.80

GROUP D

1.	174.47	218.26	192.96	188.01	25.53	35.74	38.29	35.74	2.79	4.70	5.21	5.78
2.	77.97	88.84	89.24	89.27	14.66	14.66	16.00	18.66	2.89	3.29	4.51	3.96
3.	100.91	90.68	93.41	88.63	19.09	21.82	26.59	28.87	2.88	2.42	2.33	2.08
4.	117.80	142.08	135.78	140.80	15.95	20.42	22.97	21.17	5.23	5.68	6.03	5.60
5.	107.30	131.03	120.72	124.14	15.95	22.97	25.53	29.36	3.25	3.51	3.45	3.65
6.	183.33	169.62	179.48	148.08	21.33	25.33	28.66	36.00	4.04	3.83	4.28	3.35
7.	91.60	122.08	90.55	91.74	13.40	20.42	21.70	24.26	2.29	2.71	2.05	2.08
8.	156.87	173.00	125.03	147.26	18.66	29.33	32.66	33.33	3.70	3.63	2.56	3.08
9.	118.68	117.50	98.09	103.96	10.66	10.66	10.66	13.33	3.52	3.36	3.01	3.98
10.	167.00	163.09	193.04	190.43	25.50	31.91	34.66	39.57	3.92	3.83	5.50	5.85

SUMMARY

S U M M A R Y

Despite much emphasis being placed on the link between an elevated fasting lipid lipoprotein level and atherosclerosis, it has also been observed that a large number of normocholesterolaemic subjects are equally affected by the atherosclerotic process. Thus it is evident that fasting lipid levels do not reflect the true risk of an individual. Some hyperlipoproteinaemias are the direct result of primary defects in the metabolism of lipoprotein particles. Other hyperlipoproteinaemias are secondary, that is, the elevated plasma lipoprotein level occurs as part of a constellation of abnormalities caused by an underlying disorder in a related metabolic system, such as thyroid hormone deficiency or insulin deficiency.

The present work comprised of studying the fasting lipid lipoprotein profile as well as postprandial changes induced in it after ingestion of a single high - cholesterol test diet (comprising of two boiled eggs and 250 ml of sweetened, whole fat buffalo milk) in 13 male and female subjects of endocrine and metabolic disease (Group A), 8 male and female subjects of chronic liver disease (Group B), 9 male and female subjects of chronic renal insufficiency (Group C), and 10 male subjects of chronic obstructive pulmonary disease.

Fasting blood samples, drawn after a 12 - 14 hour

overnight fast were withdrawn in the morning. Then the test diet was given and 1, 2, and 3 hour postprandial blood samples were also withdrawn and analysed for various lipid-lipoprotein fractions. The results of the analysis are summarized hereunder:

Changes in Group A.

There was a fall in serum total cholesterol (STC) concentration in group A patients 1 hour after ingestion of the test diet, and then a rising trend was noticed at the second and third hours - being especially marked in the NIDDM subgroup. In contrast, patients of IDDM showed a trend wherein the 1 hour STC rose above the fasting value, and continued to rise at 2 and 3 hours. The differences in STC values between the NIDDM and IDDM subgroups at fasting, 1 hour, 2 hours and 3 hours postprandial were all found to be statistically significant ($P \leq 0.05$).

The trend in low-density cholesterol concentrations was found to mirror closely the trend seen in STC concentrations, both overall as well as in the IDDM & NIDDM subgroups, with the differences between the two subgroups being statistically significant ($P \leq 0.05$) at all except for the third hour. Serum triglyceride levels demonstrated a sustained rise from fasting to 3 hour postprandial interval - with the difference at three hours between the two subgroups being statistically significant ($P \leq 0.05$).

Changes in Group B.

The mean fasting STC was lowest in group B patients amongst all the four disease groups studied. However, all eight patients in this group showed a rise in STC level at 1 hour. Two distinct trends were noticed in the changes in LDL concentration in group B patients. Majority of the patients showed a rise in LDL levels at one hour and continued to show a further rise at 3 hours. A minority of the patients, however, showed a fall in LDL at 1 hour, and continued to show a further fall at three hours. These differences however, were not statistically significant.

Changes in Group C.

Highest fasting as well as postprandial levels of STC were observed in group C, although the postprandial rise in STC was slight (maximum 9% at 3 hours).

This was the only group in which HDL - c showed a marked rise of almost 40 % over the basal level; whereas in group A, B and D patients, HDL - c had shown minimal variability from fasting to postprandial phase.

Low-density cholesterol concentration demonstrated a steady decline from fasting to 3 hour postprandial phase.

Highest fasting and postprandial levels of STC were observed in group C patients of nephrotic syndrome. The changes however, were not statistically significant.

Changes in Group D.

No statistically significant changes were seen in STG, HDL - c, and LDL - c in COVID patients, and factors like alcohol intake, age, smoking and secondary infection did not appear to influence any of the lipid parameters studied.

The 3 hour STG levels represented a rise of 55 % over the fasting level, which was the greatest amplitude of rise in STG following ingestion of the test diet amongst the four disease groups included in this study. As no such comparative prior studies have been done on COVID patients, it was strongly urged that further studies with larger sample groups be carried out to elucidate the qualitative and quantitative significance of these changes .
